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TUBERCLE-LIKE STRUCTURES IN HUMAN GOITERS *

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In the routine microscopic examination of goiters removed at operation, one occasionally finds small nodules which are composed of epithelioid cells and giant cells. These nodules occur in the diffuse enlargements of the gland as well as in the circumscribed, nodose hyperplasias. In the nodose goiters, they may be located in the nodes or outside in their vicinity in which location they are most frequent. A considerable literature has been devoted to the nodules, and because of their morphologic similarity to miliary tubercles they are usually considered as such. In the older literature on the morbid anatomy of the thyroid gland, tuberculosis is described as being rare. Rokitansky never saw tuberculosis of the thyroid, and according to Virchow no other gland is as seldom affected by tuberculosis as is the thyroid. In miliary tuberculosis, however, the thyroid frequently is the site of tubercles which do not differ from the tubercles in other organs except that tubercle bacilli are scanty (Fraenkel [1]). In the chronic forms of tuberculosis, involvement of the thyroid unquestionably is rare. Thus, in ninety-four cases of chronic pulmonary tuberculosis, Chiari [2] found tubercles in the thyroid only four times (4 per cent). Hegar [3] examined the thyroid in 1,563 autopsies on tuberculous patients. He saw microscopic evidences of tuberculosis in only 0.4 per cent. This excludes cases of acute miliary tuberculosis. The infection of the thyroid with the tubercle bacilli may take place by way of the blood stream or lymph stream or by way of an adjacent tuberculous organ.

Contrary to the dead house experience of a relative immunity of the thyroid to tuberculosis, which seems to be supported by some experimental observations, tubercles in goiters from patients with no other signs of an active tuberculosis have frequently been described. In practically all of the cases the tubercles were observed incidentally. The patients recovered quickly from the operation, and if followed over a sufficient length of time were found not to show any other signs of

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1. Fraenkel, E.: Virchows Arch. f. path. Anat. **104**:58, 1886.
2. Chiari, H.: Wien. med. Jahrb. **69**:119, 1878.
3. Hegar: Inaug. Diss., Kiel, 1891.

tuberculosis. The frequency of this so-called "benign tuberculosis of the thyroid" varies. In a material of 1,200 goiters, Coller and Huggins [4] saw tubercles five times (0.4 per cent). In 90 cases Marcuse [5] observed 2 tuberculous goiters. In Smith and Leech's [6] series of 1,500 goiters, there were 3 with tubercle-like nodules (0.25 per cent). In Uemura's [7] statistics, which are based on 1,400 goiters, the frequency of tuberculous changes is given with 1.7 per cent, while Werdt [8] found them three times in 144 cases of simple goiter (0.25 per cent) and once in 28 cases of exophthalmic goiter.

The majority of the authors state that the tubercles of the goiters are located in the stroma and in the follicles. The tubercles consist of epithelioid cells which are often surrounded by a zone of lymphocytes. There is a varying number of giant cells which are usually of Langhans' type. Caseation is rare, and if present is insignificant. The nodules are embedded with much dense fibrillar connective tissue, and it is this fibrosis that causes the firmness of the gland that makes one suspicious of a malignant tumor.

Few of the investigators were successful in demonstrating acid-fast bacilli in the lesions; if present, they were scanty. According to Hedinger,[9] dissolving of the gland with antiformin greatly facilitates the detection of the micro-organisms, but Mosiman [10] complained that the acid-fast granules and shrunken structures obtained by this method are difficult to identify as tubercle bacilli. Most of the authors, therefore, resort to the histologic picture as sufficient proof of the tuberculous nature of the condition, believing that the benign character of the lesion is due to the low virulence of the bacilli or to infections with such small numbers of bacilli that they escape microscopic observation, or that the lesion is not the result of the tubercle bacilli themselves but of toxins liberated in some other parts of the body.

The fact that the clinical history often shows no signs of tuberculosis in spite of the changes in the thyroid, which sometimes are rather extensive, and the failure to demonstrate the micro-organisms cast doubt on the tuberculous nature of many of the cases of so-called benign tuberculosis of the thyroid. It is the purpose in this paper to show that in the thyroid may occur nontuberculous lesions that are similar to tubercles. In a material of 300 goiters these changes were recorded four times.

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4. Coller, A., and Huggins, C. B.: Ann. Surg. **84**:804, 1926.
5. Marcuse, E.: Med. Klin. **24**:775, 1928.
6. Smith, L. W., and Leech, J. V.: S. Clin. North America **8**:185, 1928.
7. Uemura, S.: Deutsche Ztschr. f. Chir. **140**:242, 1917.
8. Werdt, V.: Frankfurt. Ztschr. f. Path. **8**:401, 1911.
9. Hedinger, E.: Deutsche Ztschr. f. Chir. **116**:124, 1912.
10. Mosiman, R. E.: Surg. Gynec. Obst. **24**:680, 1917.

REPORT OF CASES

CASE 1.—*History.*—A student nurse, aged 22, showed clinical symptoms of a mild thyrotoxicosis of one year's duration. The basal metabolic rate was plus 25. The history was negative for tuberculosis. Physical and roentgen examination of the chest gave negative results. Partial lobectomy was performed. The portion of gland that was removed contained several nodes from 1 to 5 mm. in diameter, which were rich in colloid. The intervening thyroid tissue was very firm and a light grayish brown.

Microscopic Examination.—The gland contained many nodules that were surrounded by thick capsules of fibrillar connective tissue. The smaller nodules were composed of small follicles which contained little colloid and were lined by a high cylindric epithelium. The larger nodules were made up of medium-sized and large follicles filled by thick colloid and lined by a flat epithelium. In places the epithelium was thrown up to short papillary infoldings and assumed cuboidal or cylindric shape. Outside the nodules the thyroid showed a lobular structure, the lobules being separated by a varying amount of fibrillar connective tissue. The majority of the lobules were formed by medium-sized, colloid-filled follicles with a low cuboidal lining. Some of the lobules contained follicles of irregular shape in which the colloid was replaced by a pale-stained material. The lining was cuboidal or cylindric, with an occasional papillary infolding. Here and there the lumen of a follicle was filled with desquamated round or oval cells which had an ample oxyphilic cytoplasm and light-stained, round or oval nuclei. These cells sometimes fused together into a single protoplasmic body from which fine processes extended to the epithelial lining.

A striking feature was the presence in the stroma of numerous well defined and sharply circumscribed nodules. These nodules, which were composed of light-stained cells, were scattered throughout the gland but were not found inside the nodules formed by the modified thyroid tissue. The nodules lay single or in groups, the largest of which had the size of a lobule. The groups were surrounded by much fibrillar connective tissue, which was connected with the stroma. In the periphery or in the center there was often an accumulation of lymphocytes (fig. 1). The cells of the nodules possessed an ample oxyphilic cytoplasm. Their shape was oval, and their nuclei contained a scanty, finely granular chromatin net and one or two distinct small nucleoli. There were many cells with multiple nuclei arranged peripherally about a homogeneous or finely vacuolated center. The nuclei showed the same structure as in the cells with a single nucleus.

Connective tissue stains, in particular Mallory's aniline blue stain, demonstrated about the nodules a capsule of fibrillar connective tissue. This capsule contained blood capillaries which encircled the nodules much as they did the follicles. The connective tissue fibrils did not extend inside the nodules. The Mallory stain also brought out another interesting feature, namely, the presence between the epithelioid cells of a substance that stained a bright orange yellow or red, as did the colloid in some of the follicles. The substance appeared as deeply indented, drawn out or lancet-shaped bodies, which were wedged in between the cells or enclosed in a large multinucleated cell.

A study of the slides revealed transitional stages between the follicles and the cellular nodules of the stroma (figs. 2 and 3). The swelling and desquamation of the follicular epithelium already described were the initial stage. Later, the lining epithelium showed the same structural changes as did the cells lying free in the lumen. Some of the cells fused together to form giant cells. The follicle

filled by the large oxyphilic cells and by giant cells resembled a young tubercle. There was still the layer of fibrillar connective tissue with the characteristic arrangement of the capillaries about the nodule, and there were still the débris of inspissated colloid between the cells, indicating the origin of the nodules from follicles. The picture later became more complicated by fibrillar connective tissue growing into the nodules and replacing them more and more. Thus, finally

Fig. 1 (case 1).—A group of fully developed nodules surrounding a center of lymphoid tissue. There are many epithelioid cells and giant cells. In the periphery single follicles are seen taking part in forming the nodules. The nodules are surrounded by fibrillar connective tissue. The whole area represents a lobule.

there was a dense scar which passed into the increased interstitial tissue. Lymphocytes may take part in the transformation of the follicles, though their share is limited.

Caseation could not be observed, and the most careful search for tubercle bacilli in thin and thick sections and in antiformin-treated material was negative.

The transformation of follicles into tubercle-like nodules may affect both fully developed, mature follicles and small and newly formed ones. The nodules resulting from the young follicles are small, and since these young follicles lie close together, separated only by a scanty stroma and capillaries, a group of transformed follicles may appear as a single large epithelioid cell nodule into which capillaries extend.

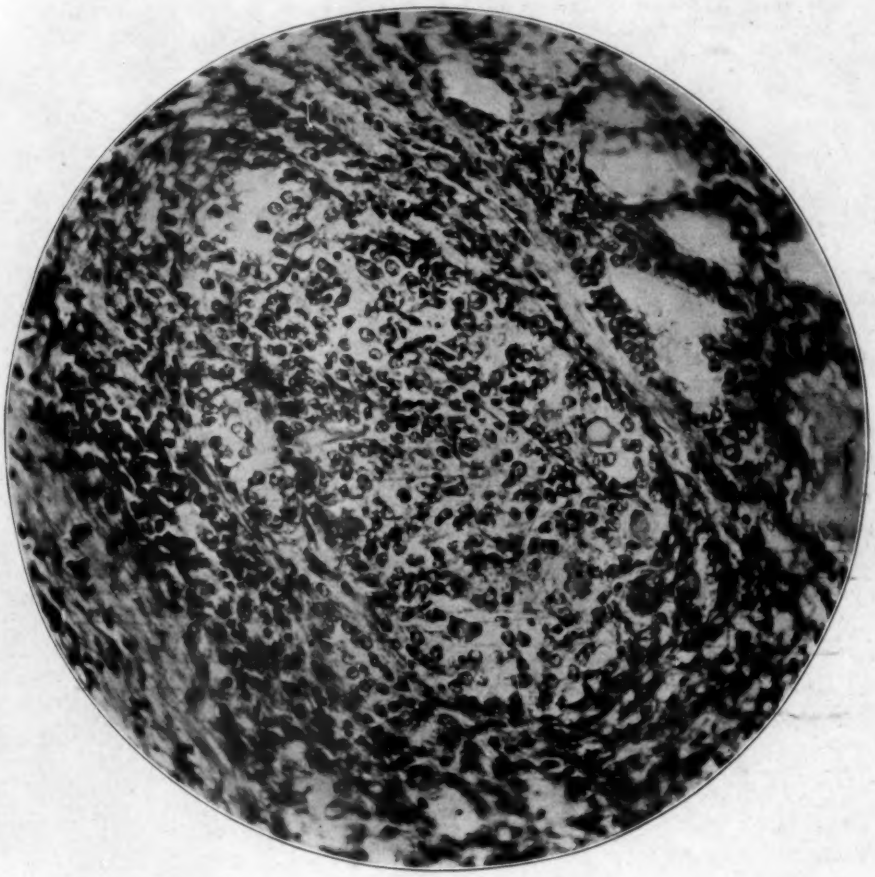

Fig. 2 (case 1).—An early stage of the involutional changes which lead to tubercle-like changes. In the left outer portion of the picture is seen the capsule of a node. Closely adjacent to it is a group of small follicles in some of which colloid is still present. There are transitions between the low cuboidal epithelium and larger cells with a distinct cytoplasm and oval nuclei. The follicles are beginning to lose their distinct outlines.

CASE 2.—*History.*—A white woman, aged 37, had thyrotoxic symptoms of moderate severity for over a year. She had lost 25 pounds (11.3 Kg.) during the last six months. The basal metabolic rate was plus 35. She had never been sick before, and had two healthy children, 7 and 4 years of age. The thyroid was

moderately enlarged and very firm. Partial lobectomy was performed. The portion of gland that was removed weighed 40 Gm. and contained many nodules from 5 to 20 mm. in diameter. Roentgen examination of the chest was negative.

Microscopic Examination.—The gland was studded with numerous nodules between which very little unchanged thyroid tissue was left. The nodules were composed of very large, colloid-filled follicles with a low cuboidal epithelial lining. There was a marked epithelial proliferation in the form of cushion-like infoldings lined by cylindric epithelium and made up of very small follicles. Many of the large follicles showed recent or old hemorrhages with iron pigment in the epithelium.

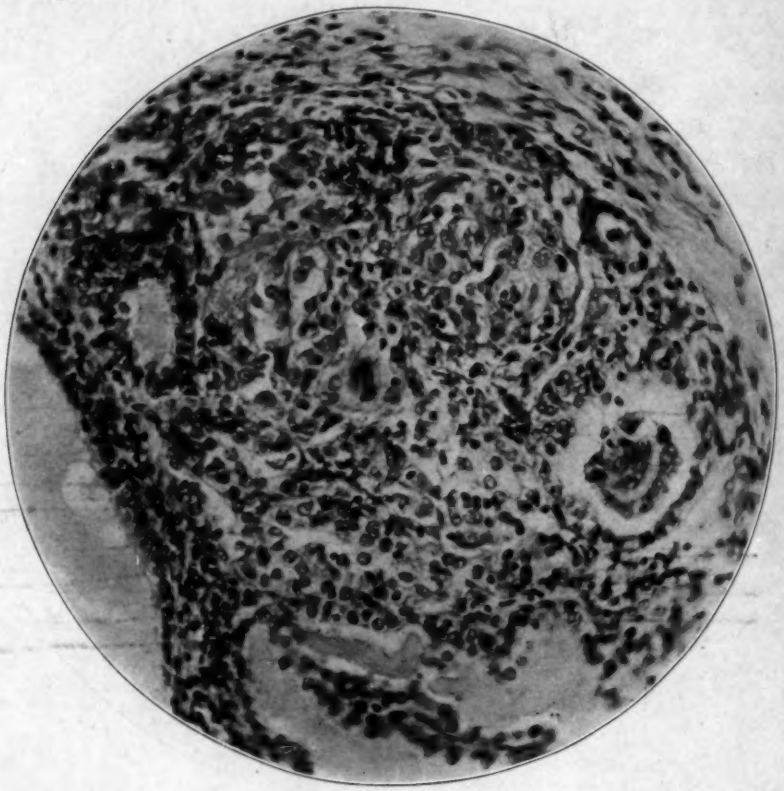

Fig. 3 (case 1).—The transformation of the follicle into a tubercle-like nodule has advanced further. Near the center of the field are seen oval cells with an ample cytoplasm. They form a distinct nodule. In the center is a giant cell; in the right lower quadrant, desquamated cells in the lumen of a follicle. They surround a giant cell.

The scanty glandular tissue between the nodules was composed of medium-sized colloid-filled follicles. There were many intralobular nodules which consisted of epitheliod cells and giant cells and which were surrounded by a zone of lymphocytes. In the periphery of the nodules were colloid-filled follicles, and one could follow their gradual transformation into the nodules in the same man-

ner as in the first case. Some of the largest nodules measured several millimeters in diameter (fig. 4). There was no caseation, and stains for tubercle bacilli did not show any micro-organisms. The changes were restricted to the glandular tissue outside the nodes of thyroid tissue.

CASE 3.—*History.*—A white woman, aged 25, had had enlargement of the thyroid for six years, and tachycardia at times for one month. There was no tremor, no nervousness, no loss of weight and no cough or expectoration. The family history was negative, and both parents were living and well. Examination

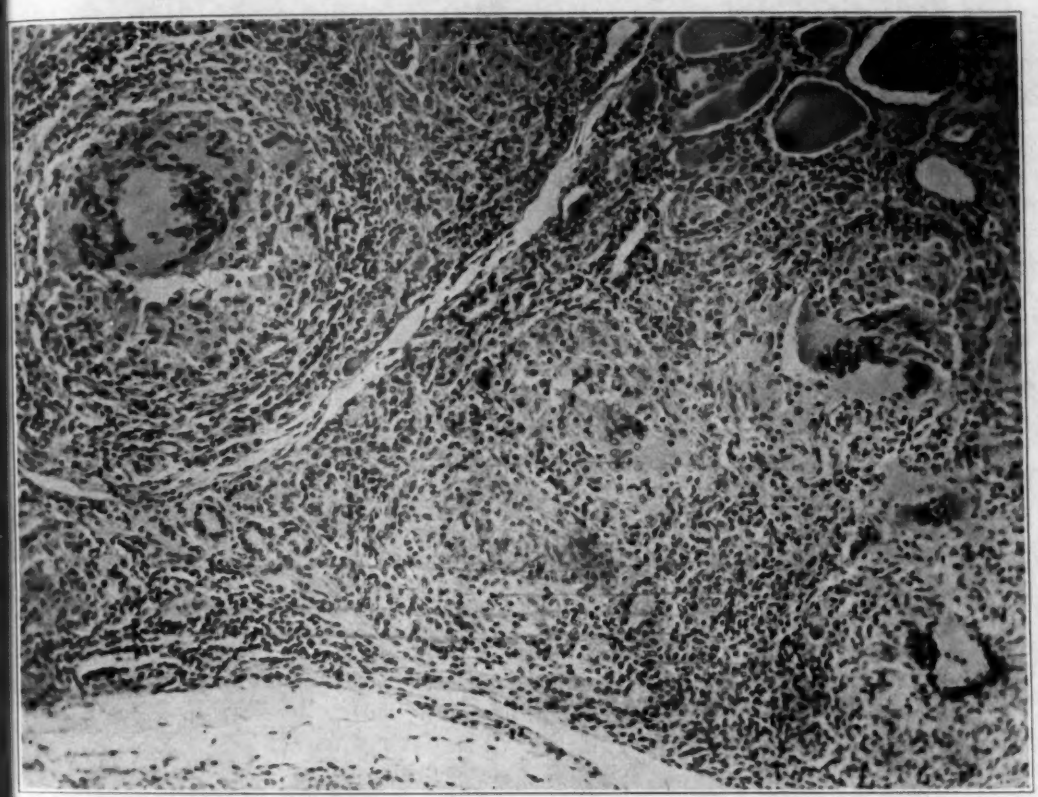

Fig. 4 (case 2).—Several nodules of epithelioid cells and numerous giant cells. The nodule in the left upper quadrant still shows its origin from a follicle.

of the chest gave negative results. Both lobes of the thyroid were slightly enlarged. The basal metabolic rate was plus 18. At operation, a small adenoma about 4 cm. in diameter was removed with some adjacent thyroid tissue.

Microscopic Examination.—The node was composed of small follicles which had a low cuboidal lining and were filled with oxyphilic colloid. The follicles were separated by thin strands of fibrillar connective tissue which in places became abundant and hyalinic. In the center of the node there were several circumscribed accumulations of pale-stained oval or polyhedral cells. The largest of these accumulations measured about 1 mm. in diameter. There were many

multinucleated giant cells. In the center of some of the accumulations there were many slender needles of fatty acid crystals. Some of the light-stained cells contained dark brown pigment granules. The follicles adjacent to these areas showed changes which suggested their gradual transformation into the nodules of epithelioid cells. There was swelling, desquamation and proliferation of the epithelium and the formation of large cells with many nuclei.

CASE 4.—*History.*—A white man, aged 26, lost 18 pounds (8.2 Kg.) in two months. He had had enuresis for two years and nervousness for from three to four years. There was increasing tremor of the hands, and generalized weakness. The appetite was good. The previous history was unimportant, except for tonsillectomy, herniotomy and appendectomy. The patient had had a chronic cough for six months. Roentgen examination of the chest gave negative results. There was marked pulsation of the thyroid, especially of the right lobe. The basal metabolic rate was plus 26; the pulse rate, 108; blood pressure, 146 systolic and 58 diastolic. The portion of the thyroid that was removed weighed 40 Gm. It was uniform and moderately firm.

Microscopic Examination.—The gland was uniformly composed of medium-sized colloid-filled follicles. Here and there one found a slight hyperplasia of the epithelium and a short papillary infolding. The lobules were separated by a stroma, which did not exceed the normal amount. A few of the lobules contained between their follicles small nodules of epithelioid cells and giant cells surrounded by lymphocytes. The origin of the epithelioid cells and giant cells could be traced to the follicular epithelium, as has been previously described.

COMMENT

The histologic changes in the three cases of nodose goiter and in the case of diffuse goiter are identical with those described as a benign, sclerosing form of tuberculosis of the thyroid. There are the circumscribed nodular accumulations of epithelioid cells and giant cells and the peripheral zone of lymphocytes and of dense fibrillar connective tissue. In none of the cases was there any sign of caseation or of other regressive changes. The absence of caseation also is emphasized by Budd and Williams,[11] Smith and Leech,[6] Wegelin [12] and others. In some of their cases Hedinger [9] and Uemura [7] observed caseation which, however, was usually insignificant.

Is the histologic picture in itself a sufficient proof of the tuberculous etiology? This question is justified because, like many other observers (Budd and Williams,[11] Moschcowitz,[13] Nather,[14] Arnd,[15] Wegelin [12] and others), I was unable to find acid-fast bacilli. All these observers based their diagnosis on the histologic picture, disregarding the nega-

11. Budd, S. W., and Williams, C.: Tuberculosis of the Thyroid Gland, J. A. M. A. **92**:1741 (May 25) 1929.

12. Wegelin, C., in Henke and Lubarsch: Handbuch der speziellen pathologischen Anatomie und Histologie, Berlin, Julius Springer, 1926, vol. 8, p. 125.

13. Moschcowitz, A.: Ann. Surg. **79**:315, 1924.

14. Nather, K.: Mitt. a. d. Grenzgeb. d. Med. u. Chir. **33**:375, 1921.

15. Arnd, C.: Deutsche Ztschr. f. Chir. **116**:7, 1912.

tive result of the bacterioscopic examination. Very similar cellular reactions, however, occur not only in other infections but also in foreign body granulomas, and if these foreign bodies, cellular or fibrillar débris or inspissated secretions, have disappeared, the differential diagnosis may offer great difficulties. Hence, the demonstration of the bacilli is of paramount importance. A few investigators found the bacilli, e. g., Ruppaner [16] in one of three and Smith and Leech in two of three cases. Most successful of all was Hedinger, who detected the micro-organisms in nine of ten cases. He used the antiformin method. I also have tried this method. Blocks of thyroid tissue 2 cm. square were cut up on the freezing microtome into sections from 35 to 50 microns thick. The entire group of sections were collected and dissolved with antiformin. After centrifugation the sediment was spread on a large number of slides and stained after Ziehl-Neelsen. The result was negative. As far as the thyroid is concerned, there is one objection to this method. Inspissated colloid, which is rich in lipoid material, as shown by its affinity to the lipoid stains, may retain the fuchsin almost to the same extent as tubercle bacilli. Débris and small splinters of this acid-fast colloid present in the sediment of the dissolved thyroids can easily be mistaken for tubercle bacilli. Even in sections, the splinters of colloid wedged in between the cells or enclosed in giant cells may resemble acid-fast bacilli.

The negative or doubtful result of the bacterioscopic examination cannot be considered absolute proof against the tuberculous nature of the lesions under discussion. It is well known that in certain forms of tuberculosis the demonstration of the bacilli is exceedingly difficult. In these cases, however, the clinical course, the association with other manifestations of tuberculosis and the result of guinea-pig inoculations confirm the diagnosis. No records on animal inoculations with material from benign tuberculosis of the thyroid are on hand. As mentioned previously, this condition is recognized only under the microscope, and the gross appearance of the gland is little suggestive of it. After the histologic examination is completed, the fresh material usually is no longer available.

In the introduction I have mentioned that autopsy experience and the result of experimental studies suggest a remarkable resistance of the thyroid against tuberculosis. There is the possibility that goitrous changes may increase the susceptibility of the thyroid to tuberculosis. Goiter is not common in tuberculous patients. The thyroid of the people who die from tuberculosis is usually small, atrophic and fibrotic. If advanced tuberculosis is associated with a goiter, tuberculous changes in the thyroid are not more common than they are in the nonhypertrophic

16. Ruppaner, E.: Frankfurt. Ztschr. f. Path. **2**:514, 1909.

gland. In only one of eighteen patients who had died from ulcerative pulmonary tuberculosis and whose thyroid contained nodes was I able to find tubercles between the nodes.

None of the four patients whose goiter on microscopic examination showed changes suggestive of tuberculosis revealed any other manifestations of this disease. The anamnesis and the physical signs were negative, as was the roentgen examination of the chest. There was nothing in the clinical picture indicating the peculiar type of goiter. The patients showed a mild hyperthyroidism, which was greatly ameliorated by the operation. The postoperative course was uneventful, and when later heard from, the patients were in excellent health. Similar experiences have been reported by Budd and Williams,[11] Neuhof,[17] Smith and Leech,[6] Creite,[18] Wegelin [12] and, in the majority of their cases, also by Nather,[14] Mosiman [10] and Hedinger.[9] Even if the patients years ago had a cervical lymphadenopathy or a pleuritis or complained of cough or showed other signs of an old and silent tuberculosis this would not necessarily speak in favor of the tuberculous nature of the lesions in the goiter, because both conditions are so common.

Many authors emphasize the benign nature of the tuberculosis of the thyroid. Nather [14] considered the changes the result of transient invasions of the blood stream by tubercle bacilli without clinical manifestations. In order to overcome the negative results of the bacterioscopic examination, some authors resort to the explanation that the nodules in the thyroid are not produced by the tubercle bacilli themselves but by their toxins liberated in some other places of the body. From where do the tubercle bacilli and from where do their toxins come, if there is no indication of any other tuberculous lesion in the body? The process in the thyroid is progressing because one can see all the stages of tubercle formation.

These considerations induce one to look for another explanation of the tubercle-like structures in goiters. There are only two authors to question the tuberculous etiology, namely, Landois [19] and Wilke.[20] They expressed the belief that the giant cells are foreign body giant cells about fragments of colloid. In Wilke's [20] case there were, however, no epithelioid cell tubercles.

The histologic descriptions and the photomicrographs of the cases that I have studied indicate that the epithelioid cells and giant cells are not derived from the histiocytic elements of the stroma but are of epithelial origin. The sequel of events is as follows: First there is

17. Neuhof, H.: Ann. Surg. **79**:313, 1924.
18. Creite: Beitr. z. klin. Chir. **78**:487, 1912.
19. Landois: Arb. a. d. path. Inst. zu Tuebingen, 1914, vol. 9.
20. Wilke: Virchows Arch. f. path. Anat. **211**:165, 1913.

desquamation of the follicular epithelium. The desquamated cells swell up, their cytoplasm becomes slightly oxyphilic and the nuclei assume an oval shape. The free cells resemble epithelioid cells. The number of these cells increases, some fuse together and form multinucleated elements, and finally the cells still attached to the wall undergo similar changes. Thus, the follicle is gradually transformed into a nodule composed of epithelioid cells and giant cells. In the earlier stages there are no reticulin fibers between the cells, an important difference from a mesenchymatous tubercle, which is characterized by an intercellular reticulin net. Later, connective tissue grows in and obscures the histiogenesis. This explanation of the histiogenesis of the tubercle-like nodules in the thyroid has been previously emphasized by Corneil and Ranvier,[21] Baumgarten, Ruppaner and others, who believed in their tuberculous nature. In nonspecific chronic inflammations of the thyroid, in particular in Riedel's struma, enormous numbers of epithelial giant cells may be present.

A rudimentary transformation of thyroid follicles into tubercle-like structures in goiters is frequently encountered. Simmonds[22] described such a transformation inside of large lymph follicles which invade the glandular follicles and separate their epithelium into small groups. These changes undoubtedly are involutional. It is this explanation that I advance also for the fully developed nodules; namely, that they are the result of a noninflammatory swelling, degeneration and desquamation of the follicular epithelium that is followed by the ingrowth of fibrillar connective tissue. The fibrous replacement is favored by the fact that the follicles of the thyroid do not possess a membrana propria. What may cause this form of focal involution of newly formed and old follicles is difficult to determine. As mentioned, these changes are much more frequently found in the periphery of and closely adjacent to the nodose hyperplasias than inside the nodes or in the diffuse enlargements. In serial sections of one of my cases I found in the center of some of the tubercle-like nodules clusters of fatty acid needles, which supports the conception of the degenerative nature.

There are no characteristic clinical signs associated with the goiters containing the focal tubercle-like areas of involution, except that the glands are often very firm. The patients may show severe symptoms of exophthalmic goiter or a moderate or slight hyperthyroidism or no toxic symptoms at all (Plummer and Broders,[23] Frassi,[24] Mosiman,[10] Coller

21. Corneil, V., and Ranvier, L.: Manual d'histologie pathologique, Paris, 1876.

22. Simmonds, M.: Virchows Arch. f. path. Anat. **211**:73, 1913.

23. Plummer, W. A., and Broders, A. C.: Minnesota Med. **3**:279, 1920.

24. Frassi, L.: Deutsche Ztschr. f. Chir. **213**:416, 1929.

and Huggins,[4] Marcuse,[5] Uemura,[7] Neuhof [17]). A review of the literature shows that the nodules are seven times more common in females than in males. Most of the patients are between 30 and 50 years of age.

I do not deny the existence of a true tuberculosis of the thyroid and of a tuberculous strumitis (Ruppaner [16]). The literature contains reports of a number of well proved cases. There are small or large, discrete, caseating tubercles or conglomerated tubercles with extensive caseation or cold abscesses. Associated with these changes are tuberculous lesions of the other organs, especially of the lungs, bones or cervical lymph glands. In the literature on tuberculosis of the thyroid these true forms are often grouped together with the tubercle-like changes obscuring the differences between the two conditions (Jones,[25] Nather,[14] Marcuse [5] and others). Before making the diagnosis of tuberculosis of the thyroid one should keep in mind that there occur in goiters tubercle-like structures with extensive fibrosis which are not due to an infection with Koch's bacillus but are the result of focal involutional changes.

SUMMARY

In three cases of nodose goiter and in one case of diffuse goiter with mild hyperthyroidism there were found in the removed thyroid tissue nodular structures composed of epithelioid cells and giant cells which resembled miliary tubercles. The origin of these cells could be traced to the follicular epithelium. The patients showed no other signs of tuberculosis and made an excellent recovery. There was no caseation in these nodules, but much fibrosis about them. In spite of a most careful search, tubercle bacilli could not be demonstrated.

The explanation is advanced that the tubercle-like structures are the result of noninfectious focal involutional changes of newly formed and old follicles. These nontuberculous changes should be separated from true tuberculosis of the thyroid.

25. Jones, T. B.: Am. J. Surg. **7**:629, 1929.

POSTOPERATIVE URINARY INCONTINENCE

REVIEW OF LITERATURE AND REPORT OF CASES *

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Loss of voluntary control of the bladder after prostatectomy is very distressing to the patient, as he feels his postoperative plight much more keenly than his preoperative suffering. This is an extreme disappointment to the surgeon as it mars and discounts an otherwise technically perfect operation. The occurrence of incontinence of urine following prostatectomy is more frequent than statistical and general reports would lead one to believe. Fortunately, the mastering and perfection of technic of both the suprapubic and perineal methods of prostatectomy by well trained genito-urinary surgeons has led to a marked disappearance of this very disagreeable and annoying symptom.

The mechanism of urination and the anatomic changes about the neck of the bladder and posterior urethra have been imperfectly understood until recently. During the past fifteen years, genito-urinary surgeons have displayed an increased interest in the ultimate results of prostatectomies, and this has led to numerous investigations into the causative factors of the poor functional results. In this recent period, one finds numerous observations recorded about the anatomic and functional condition of the musculature around the neck of the bladder following prostatectomy. Prior to this time, there was a decided paucity of literature dealing with this subject.

INCIDENCE

Incontinence of urine following prostatectomy has been encountered by practically every genito-urinary surgeon who has performed an extensive series of prostatectomies, irrespective of the method used. The general belief persists, and rightly so, that incontinence occurs more frequently after the perineal than after the suprapubic method. However, in the hands of surgeons specially trained in the perineal technic, the occurrence of incontinence is less than in the hands of untrained surgeons.

According to the statistical studies of various surgeons, postoperative urinary incontinence is a relatively infrequent condition. However, we

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feel that if accurate follow-up investigations were made in cases of prostatectomy, a greater percentage of urinary incontinence, either complete or partial, would be found to exist. The vagueness of the term incontinence may account for the variability of the results reported.

The necessity for a definite terminology in regard to incontinence is evident. The term true or complete incontinence implies the complete loss of control of urination and the existence of urinary dribbling at all times. The term, partial or incomplete incontinence, implies a partial or faulty control of urination with the occurrence of dribbling between urination on exertion or at the end of urination, other than the amount of leakage one ordinarily sees in a normal person when the anterior urethra is not stripped.

The degree of incontinence may vary in the same or different persons. It may be temporary or permanent and hence of slight or serious importance.

Temporary incontinence, lasting several days or weeks, is a rather frequent occurrence after a suprapubic or perineal prostatectomy, but more so after the latter method. Fortunately, the condition responds to treatment very well. The cause of such incontinence may be a slight cicatricial contraction in the prostatic urethra or about the vesical neck, and instrumental dilation at frequent intervals results in complete restoration of function. Occasionally, a temporary incontinence is associated with an anesthesia of the urethra and vesical neck which is the result of trauma incidental to the removal of the prostate. These patients are not conscious of urine passing through the urethra. If the nerve supply is intact, the sensation of urination is soon restored and control of urination reestablished.

Some patients have a slight incontinence when standing or walking for the first time. Some do not dribble when resting or reclining but on assuming an upright position, such as standing or walking, they dribble a few drops. The latter two forms of incontinence disappear rapidly as the patient gains control of urination. In the first few days of convalescence when urine is voided through the urethra, the patient should be instructed how to start and stop his stream voluntarily several times during each act of urination and to void at frequent intervals in order to improve the tone of the vesical sphincters and to facilitate control of urination. The importance of these bladder exercises has been stressed by Alexander.

Often in old and debilitated patients there may develop a terminal dribbling accompanied by a marked frequency and urgency. If this condition should persist, it may result in a true complete incontinence as the sphincteric control is gradually lost. Permanent incontinence is associated with some anatomic or mechanical defect involving both sphincters, and is the result of operative manipulation.

Incontinence may also be diurnal or nocturnal or both. Diurnal incontinence is usually partial and temporary, and manifests itself when the patient is up and about on his feet in the first few days of voiding. It responds well to therapy, such as dilatations of the posterior urethra, and disappears in a very short time. Nocturnal incontinence seldom occurs alone but is usually accompanied by diurnal incontinence, and these combined must be considered as a true or complete incontinence which is of grave prognostic significance.

Series of different types of prostatectomies have been reported by many authors with some reference to incontinence. In 1902, Parker Syms reported three cases of incontinence following thirteen perineal prostatectomies. In 1904, Watson made a very complete résumé of the results and complications in an extensive series of prostatectomies. He noted the occurrence of incontinence of urine in 3.5 per cent of a series of 530 perineal prostatectomies and 2.6 per cent of 1,086 cases in which Bottini's operation was done. He made no mention of urinary incontinence in the series of 243 suprapubic prostatectomies. Escat (1904) reported 12 cases (3 per cent) of urinary incontinence in 382 cases of perineal prostatectomies. Ruggles reported 5 cases (13 per cent) of incontinence in 39 prostatectomies, presumably of the perineal type. Pauchet reviewed a series of 50 perineal and 152 suprapubic prostatectomies but did not find any definite cases of incontinence. However, he stated that certain patients lost a little of their urine. This complication lasted several weeks or months but always disappeared. The patients who presented the symptoms of incontinence for the longest time had some affliction of the nervous system.

Ertzbischoff (1911) studied the late complications of transvesical (suprapubic) prostatectomies and found 11 cases in 1,573 operations. In most cases, the cause was a lesion of the membranous urethra which normally should be avoided. In 1912, Freyer reviewed a series of 1,000 suprapubic prostatectomies and did not mention a single case of incontinence except to state that in 1 case the patient failed to regain the power of voluntary micturition. He attributed this to a flaccid bladder paralyzed by the extreme overdistention present before the catheter was employed to relieve the condition.

In 1911, Judd reviewed a series of 532 cases, which included 323 perineal and 140 suprapubic prostatectomies for benign hypertrophy of the prostate and 50 perineal and 19 suprapubic prostatectomies for carcinoma of the prostate. He stated that urinary incontinence following prostatectomy is a rare occurrence. He did not have a case of incontinence following suprapubic prostatectomy for benign hypertrophy, although 2 patients, operated on by the suprapubic route who did not have complete control before operation, were not relieved. In 2 patients who had suprapubic operations for carcinoma, good control

of urination was present for some time after the operation, but incontinence gradually developed on recurrence of the old trouble. He stated that there were 7 cases of perineal prostatectomy with some degree of incontinence, in some of which there had been dribbling before operation. In 3 of these cases there was a history of an old syphilitic infection, but there was no evidence of syphilis at the time of operation. In addition to the aforementioned cases, there were 11 patients on whom perineal prostatectomy had been performed whose retentive power was not strong but who could hold their urine several hours before dribbling. Several patients did not have good control immediately following operation but regained it in several weeks. Some had difficulty in retaining urine when in the recumbent position. Others had good control while lying down but leaked a few drops when they were in the upright position.

Gardner, in his large series of cases, had never seen incontinence following a perineal or suprapubic prostatectomy, and he attributed this to the preservation of the compressor urethrae muscle. In a series of 450 perineal prostatectomies reported by Young, in 1911, complete incontinence—dribbling day and night—did not occur in a single instance, and only three cases of partial incontinence occurred. In the second volume (page 461) of his "Practice of Urology," he has tabulated the results of 55 cases of suprapubic prostatectomy and reported incontinence in 3 cases (5 per cent).

In Deaver's collected series of 1,734 suprapubic cases and 676 perineal cases, this complication occurred 46 times (2.6 per cent) in the suprapubic series and 36 times (5.1 per cent) in the perineal series. Forty-one of these 46 cases of incontinence following suprapubic prostatectomy are reported by one correspondent as occurring among 75 patients. McDonald mentioned 3 cases of incontinence in his analysis of the suprapubic cases in which operation was performed at St. Peter's Hospital, London.

Martin, in an analysis of the results in a series of 110 patients on whom prostatectomy was performed (55 cases each of the perineal and suprapubic method), gave definite information concerning incontinence in 50 perineal and in 46 suprapubic cases. In the perineal series, 32 patients (64 per cent) had full control of the bladder, 11 (22 per cent) partial incontinence and 7 (14 per cent) complete incontinence. In the suprapubic series, 37 (80.5 per cent) had full control, 7 (15.2 per cent) had partial control of the bladder and 2 (4.3 per cent) complete incontinence.

Hinman recorded observations based on 90 perineal and 38 suprapubic cases. He mentioned dribbling in 1 perineal case complicated by cerebral syphilis. Dribbling at the end of urination was present in 37 per cent of the suprapubic and 20 per cent of the perineal cases.

Dribbling on exertion between urination existed in 26 per cent of the suprapubic and 9 per cent of the perineal cases.

Swan reviewed the functional results of a series of 100 cases of all types of operations on the prostate and noted a restoration of urinary control to normal in 82 per cent. Analysis of his results reveals that leakage, or dribbling of urine, occurred in 7 of the 54 cases of one-stage suprapubic prostatectomy; in 1 of the 23 cases of two-stage suprapubic prostatectomy; in 5 of the 9 cases of perineal prostatectomy, and in 5 of the 14 cases of punch prostatectomy.

E. Davis reported the late results of perineal prostatectomy ascertained by questioning 100 consecutive patients in a series of 176 cases. There was no case of complete incontinence; 2 patients had a sufficient degree of incontinence to cause considerable inconvenience, and 2 others had a slight degree of incontinence. In the former (2 cases with inconvenient incontinence), each of the patients had intervals of complete dryness and the ability to start and stop the stream at will several times while voiding. However, there was a weakness of the external sphincter as indicated by leakage of small amounts of urine following undue exertion such as coughing, sneezing and sudden rising.

Cecil reported one case of incontinence in 234 consecutive prostatectomies. His series includes: 201 cases of perineal prostatectomy for benign hypertrophy of the prostate; 15 cases of suprapubic prostatectomy for benign hypertrophy of the prostate and 2 cases of suprapubic prostatectomy for carcinoma of the prostate. He does not state the type of operation following which the incontinence occurred.

The figures of Whiteside based on 1,423 cases in which prostatectomy was performed by suprapubic and perineal routes are of interest. He reported 24 cases of urinary incontinence, all of which followed perineal prostatectomies.

We have recently reviewed a series of 220 prostatectomies performed by us and noted the occurrence of incontinence of urine in 1 case (0.7 per cent) in 134 suprapubic prostatectomies and in 5 cases (5.8 per cent) in 86 perineal prostatectomies. The suprapubic case was one of partial incontinence. Of the 5 perineal cases, there was complete incontinence in 2 and partial incontinence in 3.

Here and there in the literature one finds isolated reports of a case of incontinence following prostatectomy associated with some abnormal change in the musculature about the vesical neck. Fullerton reported 3 cases of stenosis of the internal orifice of the bladder after suprapubic prostatectomy, and in 2 there was incontinence.

ANATOMY

Before a discussion of the nature of the changes in the musculature about the vesical neck and the posterior urethra following operative

intervention is undertaken, a brief description of the normal anatomic relations of these structures will aid in understanding the postoperative and pathologic observations.

Anatomists differ greatly on the exact muscular components of the sphincters of the bladder. The most accurate work in this field was performed by Wesson in 1920 and by Young and Wesson in 1921 in a comprehensive and excellent anatomic, embryologic and surgical study of the trigone of the bladder. In the following descriptions, we have drawn very largely from their studies and observations.

The Bladder.—The bladder has four coats, but for the greater part is made up of two ill defined layers of smooth involuntary muscle—an external longitudinal and an internal circular layer. The arrangement and direction of these layers are difficult to ascertain, for they change and rearrange themselves with each change in the size of the bladder. It has been agreed that the entire musculature of the bladder contracts together and thus acts as one muscle, which is called by some writers, the "detrusor of the bladder."

The Trigone.—At the base of the bladder there is a distinctly separate layer of muscle superimposed on these two layers of bladder muscle which is known as the trigonal muscle. This muscle is of mesodermal origin, while the two layers of bladder muscles are of endodermal origin. The trigonal muscle is in reality an extension of the longitudinal muscle layers of the ureters and their sheaths. The fibers that compose this muscle spread out in a fanlike direction from each ureteral orifice. Some of these fibers spread medially from each ureteral orifice, meeting and forming Mercier's intra-ureteric bar. Some fibers interlace in the middle of the trigone with the corresponding fibers of the other side, and still others pass downward into the urethra to form the muscles of Bell. The muscles of Bell on each side apparently converge at the vesical neck to form a thickened layer of muscle passing over the posterior edge of the vesical orifice known as the uvula of Lieutaud.

The mucous membrane of the trigone differs markedly from that of the remainder of the bladder in that in the former instance it is far more intimately adherent to the subjacent tissues and does not present any rugae when the bladder is empty, thus preventing any prolapse of the mucous membrane into the vesical orifice during micturition.

The Internal Vesical Sphincter.—The internal vesical sphincter is made up of muscle fibers from the external longitudinal and internal circular layers of the bladder musculature. Most of the fibers from the external longitudinal layer on the posterior surface of the bladder pass downward to end abruptly in the region of the vesical neck. Other fibers from this layer pass along the posterior surface of the bladder to the vesical neck where they diverge slightly and pass downward and

forward on either side in the form of muscular bands. These bands swing medially to form a continuous loop or arch about the urethra at its very upper limit just beyond the prostate. This muscular loop is known as the external arcuate muscle of the vesical orifice. The fibers from the internal circular layer of the bladder pass around the bladder neck down to the vesical orifice at which point it becomes a thin band lying inside the loop formed by the fibers from the external longitudinal layer (as previously described). The inner thin loop is known as the internal arcuate muscle of the vesical orifice. The formation of this muscle is dependent on some of the fibers of the internal circular layer on the posterior surface of the bladder passing downward and forward in an oblique direction in the form of a loop or arch in front of the urethra in the region opposite the verumontanum (fig. 1).

There are elastic tissue fibers interspersed among these smooth muscle bands at the vesical orifice, and, in addition, some of these

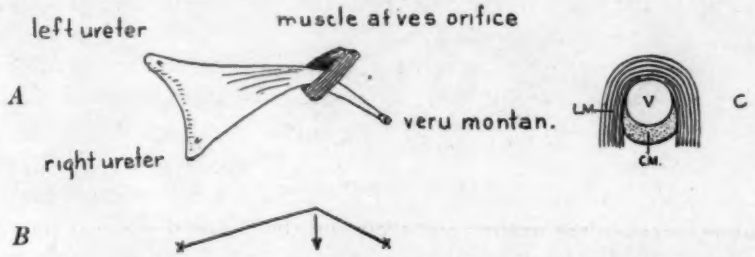

Fig. 1.—Diagrams to show the effect of contraction of the trigone in opening the internal vesical sphincter. *A* indicates the trigonal muscles passing through the lateral muscles of the sphincter and over the uvula vesicae; *B*, the effect of contraction of the arc-shaped trigonal muscle, viz., to pull down the uvula vesicae and open the sphincter; *C*, cross-section of the vesical orifice (*V*) showing the upward pull of the loop from the circular muscle (*C.M.*) and the opposing action of the longitudinal muscle (*L.M.*) loop. (After Young: Practice of Urology, vol. 1, figs. 3 and 5.)

elastic fibers from the external longitudinal layer of the bladder pass downward to form an interlacing network between the deeper layers about the vesical orifice.

The internal vesical sphincter is thus composed of two loops of smooth muscle: the external arcuate muscle of the vesical orifice derived from the external longitudinal layer of the bladder, and the internal arcuate muscle of the vesical orifice derived from the internal circular layer of the bladder. The internal sphincter is in reality a surgical designation and not an anatomic entity, since it is not a simple circular sphincter, like the sphincter ani, with an origin and an insertion in itself. Its function will be discussed later.

The External Sphincter of the Bladder.—The external sphincter is situated at the level of the triangular ligament and is composed of striated voluntary muscle. It is innervated by the internal pudic nerve. This sphincter has its origin in a group of striated muscle fibers that are slightly anterior to the external arcuate muscle of the vesical orifice at its medicolateral aspect. These fibers pass in a circular direction in relation to the urethra and at first do not surround the urethra entirely. As they pass downward and forward to the apex of the prostate, they increase in number and completely surround the urethra, and at the level of the triangular ligament they form a thick circular band with a raphé due to the interlacing of fibers from each side.

The Compressor Urethrae.—The compressor urethrae is composed of striated voluntary muscle fibers which covered the entire membranous urethra. It has the same origin as the external sphincter and is essentially the striated muscle fibers that are first posterior to and lead up to the external sphincter. In the literature there is a decided tendency to an interchangeability of the terms, compressor urethrae and external sphincter, and very often both are included under the name of either muscle. This may be easily understood when one realizes that both muscles have the same origin and innervation and essentially the same function.

Intrinsic Smooth Musculature of Posterior Urethra.—In addition to these striated muscle fibers, the urethra has a well defined internal longitudinal and poorly defined circular layer of smooth involuntary muscle which are derived from the muscle layers of the bladder and trigone. The inner longitudinal layer of smooth muscle on the anterior aspect of the posterior urethra is derived from the external longitudinal layer of the bladder, and on the posterior aspect from the trigonal muscle as it passes down over the posterior margin of the vesical orifice. The internal longitudinal muscle fibers extend down to the membranous urethra ending in the region of Cowper's glands. There are also a few circular smooth muscle fibers surrounding the urethra in the region of the vesical sphincter which are derived from the muscular components of the arcuate muscles at the vesical orifice. The prostatic urethra, for a short distance extending from the vesical orifice to a point about half way down to the verumontanum, is devoid of fibers derived from the internal circular layer of the bladder. However, Young and Wesson have pointed out that the fibers from this layer extend into the prostate gland where their course cannot be traced, and it is very likely that these circular fibers have been invaded and distorted by prostatic tubules and that the composite mass represents the prostate gland.

The two layers of intrinsic smooth muscle in the posterior urethra, together with the internal vesical sphincter, are innervated by sympa-

thetic fibers from the inferior mesenteric and from prostatic and cavernous plexuses through the hypogastric plexus.

THE MECHANISM OF URINATION

The correlation of physiologic and neuro-anatomic studies with cystoscopic and surgical observations has served to clarify the complex mechanism of urination. In this respect the observations and studies of Young and Wesson, Graves and Davidoff, Rose and Deakin, Elliot and McClintic are of great value. The nervous and musculature mechanisms involved in the act of urination are rather complicated and recently have been the subject of comprehensive study. While complete infor-

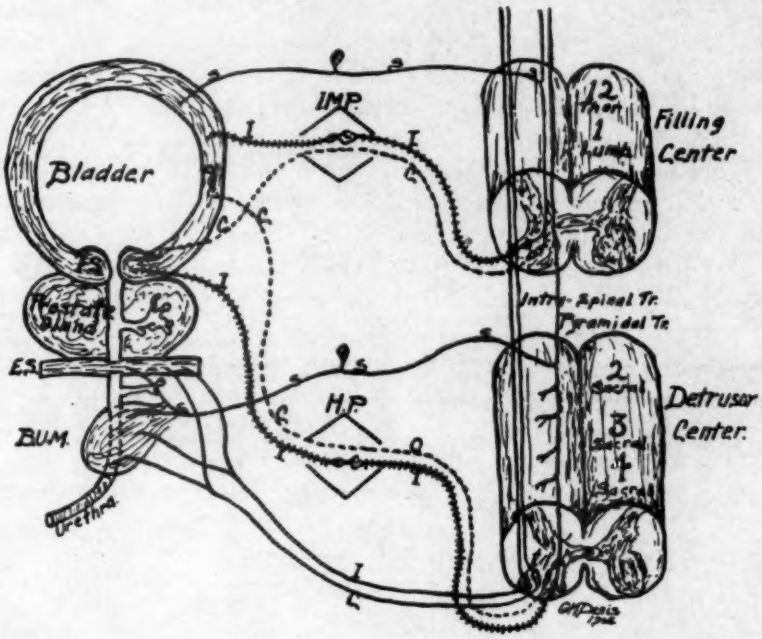

Fig. 2.—Detrusor mechanism (nerve supply). *H. P.* indicates the hypogastric plexus; *I.M.P.* inferior mesenteric plexus. The nerve fibers are indicated as: *I*, inhibitor; *C*, contractor; *I.S.*, internal sphincter; *E.S.*, external sphincter; *B.U.M.*, bulbo-urethralis muscle, and *S*, the sensory muscle. (After McClintic: J. Urol. **20**:269 [Sept.] 1928.)

mation is still lacking, several facts have been clearly established in regard to urination. In the following discussion, it is our intention to present a brief review of the accepted facts and theories concerning urination.

Nerve Supply of the Bladder (fig. 2).—Studies reveal that the bladder has a bilateral nerve supply as each half of the bladder has its own innervation. The trigone has a richer nerve supply than the

remainder of the bladder. The main nerve trunks enter the bladder in the region of the ureters after passing through the peripheral ganglions found about the base of the bladder. There are two sets of nerves supplying each half of the bladder.

1. The parasympathetic nerves, known as the pelvic splanchnic nerves or nervi erigentes, are made of fine medullated fibers which are derived from the anterior branches of the sacral plexus at the level of the second, third and possibly the fourth sacral nerves. These nerves pass to the pelvic or hypogastric plexus at the base of the bladder.

2. The sympathetic nerves (hypogastric nerves) are of the non-medullated type and arise from the white rami communicantes of the lumbar nerves. They pass through the aortic plexus to reach the inferior mesenteric ganglion. From this ganglion, two main nerve trunks (hypogastric nerves) pass down along the sides of the rectum, one on each side, to the pelvic plexus.

In the pelvic plexus, one finds that the spinal fibers unite with the sympathetic fibers, and the nerves from the pelvic plexus to the bladder are mainly nonmedullated fibers. Three ganglions of the pelvic plexus are especially concerned in the innervation of the bladder.

(*a*) The superior (or rectovesical) ganglion, which lies in front of the rectum and sends a few fibers to the superior surface of the bladder.

(*b*) The major vesicoseminal ganglion, which lies on the base of the bladder and supplies the superior, lateral and anterior bladder surfaces.

(*c*) The minor vesicoseminal ganglion, which lies on the base of the bladder but more mesial than the previous ganglion and sends fibers to the base of the bladder and to the ureters.

On reaching the bladder wall, all the nerves divide into many fine branches which are distributed to the various layers of the bladder. The nerves transmitting sensory impulses are found in all four layers of the bladder. The motor nerves relay in the ganglions and plexuses of the outer layer of the bladder and from here send fibers to the musculature of the bladder. In the submucosa are found several minute ganglions from which filaments arise and penetrate the mucosa to end between the epithelial cells. The inhibitory fibers terminate in the muscular coat.

The afferent bladder impulses reach the spinal cord through sensory nerves. The majority of the afferent impulses pass through the pelvic splanchnics (nervi erigentes) to reach the cord by way of the posterior roots of the second, third and possibly the fourth sacral nerves. A small number of these impulses are thought by some observers to pass through sensory filaments in the hypogastric plexus to reach the cord by way of the twelfth thoracic and the first and second lumbar nerves.

These sensory neurons end (*a*) in the second, third and fourth sacral segments of the cord, and (*b*) in the twelfth thoracic and first and second lumbar segments of the cord. They make connections with the motor neurones in the ventral horn cells of the cord directly as a reflex arc or by association paths as a part of a reflex system. Thus, when the posterior roots of the nerves supplying these spinal segments are stimulated, the motor fibers to the bladder in the anterior roots of the nerves are reflexly excited.

The association tracts connecting the thoracolumbar and sacral parts of the cord are the intraspinal tracts found in a solitary spinal fasciculus. The latter tract is an association path which connects not only the visceral centers of the different levels of the spinal cord but also those of the medulla oblongata, forming a continuous visceral mechanism. As McClintic points out, the mechanism so formed is protective and automatic and represents the mechanism of instincts also described as the primitive reflexes or the mass reflex system.

The efferent or motor paths from the cord to the bladder are also confined to the parasympathetic system (nervi erigentes) and the sympathetic system (hypogastric nerves). Their various pathways through the intrinsic and extrinsic ganglions and their excitator and inhibitory elements are considered later in relation to the emptying and filling mechanisms of the bladder.

In view of the foregoing observations, we can say with some degree of certainty that the spinal cord center for micturition is found in the lower part of the cord (lumbosacral region) and is more or less localized to separate segmental areas: (*a*) the center for "the bladder-filling mechanism," localized in the twelfth thoracic and first lumbar segments and controlling the sphincter area; (*b*) the center for the emptying mechanism of the bladder, localized to the second, third and fourth sacral segments and controlling the detrusor muscle. Halliburton (quoted by Graves) considered the sacral segment of the cord as the spinal center for micturition, for he maintained that the micturition reflex remains intact in animals whose cord is cut across in the lower lumbar region. Starling (quoted by Graves) expressed the belief that the lumbosacral region serves as the spinal center, since micturition is possible when the thoracic portion of the cord is severed and the reflex arcs of the lower cord are left intact.

The cerebral centers for urination are less clearly defined. Kretschmer quoted Czyhlarz and Marbury as claiming the existence of three such cerebral centers: a center in the cortex of the motor area where the arm center goes over into the leg center; a center in the corpus striatum, and a center in the optic thalmus. Tigerstedt (quoted by Graves) suggested a center in the anterior part of the sigmoidal gyrus since stimulation of this area in a cat produces contraction of the bladder

with the impulses passing through the thalamus, crura, cerebri, pons and medulla to the cord. The spinal path for motor impulses from the brain to the bladder is generally conceded to be in the posterior part of the pyramidal tract of the lateral column.

Neuromuscular Mechanism (Fig. 2).—The bladder, like the anus and the uterus, has a combined voluntary and involuntary mechanism. In the bladder, this mechanism is called the detrusor mechanism and is made up of a filling and emptying system. Both the filling and emptying mechanisms consist of an inhibiting (relaxing) and an excitator (contracting) element which are correlated. The bladder, like other viscera, has a double innervation wherein impulses transmitted through a parasympathetic system are antagonistic to those transmitted through a sympathetic system.

The filling mechanism is entirely involuntary (automatic or autonomic). The center for this mechanism is located in the twelfth thoracic and first lumbar segments of the spinal cord. The "nerves of filling the bladder" are sympathetic in character and are called the hypogastric nerves which are derived from anterior roots of the spinal nerves from the aforementioned spinal segments. These nerves pass through the inferior mesenteric ganglion and plexus to supply the bladder and internal sphincter. The inhibitory fibers relay in the peripheral ganglion (inferior mesenteric ganglion) to end in the muscular layer of the bladder. The excitator (contracting) fibers relay in the intrinsic (bladder) ganglion and supply the internal vesical sphincter. Stimulation of the "nerve of filling" produces a relaxation of the bladder wall (detrusor) and a contraction of the internal vesical sphincter.

The emptying mechanism is partly involuntary and partly voluntary. The involuntary part differs from the filling mechanism in that the center for the emptying mechanism is in the second, third and fourth sacral segments of the spinal cord, and the peripheral ganglions and plexuses are in the pelvic (hypogastric) plexus. The emptying and filling centers are connected by means of an association pathway (solitary spinal fasciculus) or an intraspinal tract of association fibers. The nerves of emptying concerned in the involuntary system are parasympathetic in character and are called the nervi erigentes (pelvic splanchnics). Inhibitory fibers of these nerves pass to the internal vesical sphincter after relaying in the peripheral ganglion (hypogastric plexus). The excitator fibers relay in the intrinsic ganglions of the bladder walls to end in the muscular coat of the bladder. Stimulation of these parasympathetic nerves of emptying causes a contraction of the bladder (detrusor) and a relaxation of the internal vesical sphincter.

The voluntary part of the emptying mechanism involves two striated muscles, external vesical sphincter (compressor urethrae) and the bulbo-urethralis (accelerator urinae) muscles, which are supplied by

the perineal branch of the internal pudic nerve, a spinal nerve. The voluntary system also has its center in the second, third and fourth segments of the spinal cord. The peripheral afferent or sensory path of the involuntary system is essentially the same, physiologically, as the involuntary system of the emptying mechanisms, for the sensory neurons from these areas make the same local connections in the second, third and fourth sacral segments, but in addition it makes connections with the sensory areas of the cerebrum.

The efferent or motor path of the voluntary system, however, differs, as in the former instance the motor neurons pass directly to the muscles without relaying in the extrinsic ganglions or ending about intrinsic ones. The excitator and inhibitory impulses to these muscles originate in the cerebrum and the spinal cord centers by way of the pyramidal tracts. The cerebral center for inhibition of the voluntary part of emptying mechanism is presumably in the frontal area. The inhibitory impulses transmitted through the pyramidal tract serve a double purpose: (*a*) They permit the voluntary muscle to relax while their functional antagonists contract, and (*b*) they inhibit reflexes. It is thought by some observers that the sensation of pain in the region of the bladder is transmitted through the pudic nerve. Stimulation of this nerve causes a contraction of the posterior urethra which is of short duration.

In other words, the detrusor mechanism is a diphasic mechanism and consists of two parts, a filling and an emptying system. The filling of the bladder is an involuntary phenomenon which requires a relaxation of the musculature to permit distention and a contraction of the interior vesical sphincter to keep the bladder closed. When the bladder is distended, the internal involuntary sphincter relaxes as a result of reflex stimulation of the spinal centers by afferent bladder impulses, and unless urination takes place further closure must be maintained by the external voluntary sphincter. The emptying of the bladder is in part involuntary and in part voluntary. The involuntary system requires a contraction of the bladder musculature and a relaxation of the internal vesical sphincter which is combined with a relaxation of the external vesical sphincter.

The Muscular Mechanism of Urination (Figs. 3 and 4).—The muscular mechanism in the act of urination functions in an orderly manner. In the normal male, micturition is voluntarily initiated. In the first motion, there is a voluntary depression of the internal sphincter and prostatic urethra by the levator prostatae (a portion of the levator ani muscle) and to a less extent by the recto-urethralis muscle. This results in a downward depression of the internal orifice and a straightening out of the curve of the prostatic urethra to overcome the resistant angle of the membranous urethra, which is depressed by the deep trans-

verse perinei muscles. The actual emptying of the bladder is the result of an involuntary mechanism which requires an inhibition (relaxation) of the internal sphincter and a simultaneous contraction of the whole bladder musculature (detrusor). This latter mechanism is dependent on afferent stimuli caused by the distention of the bladder reaching the spinal cord centers through the sympathetic system, and here, through intersegmental (reflex) connection, efferent impulses arise which cause the trigonal muscles to contract. The contraction of the trigonal muscles results in the opening of the internal sphincter and foreshortening the posterior urethra above the verumontanum. The contraction of

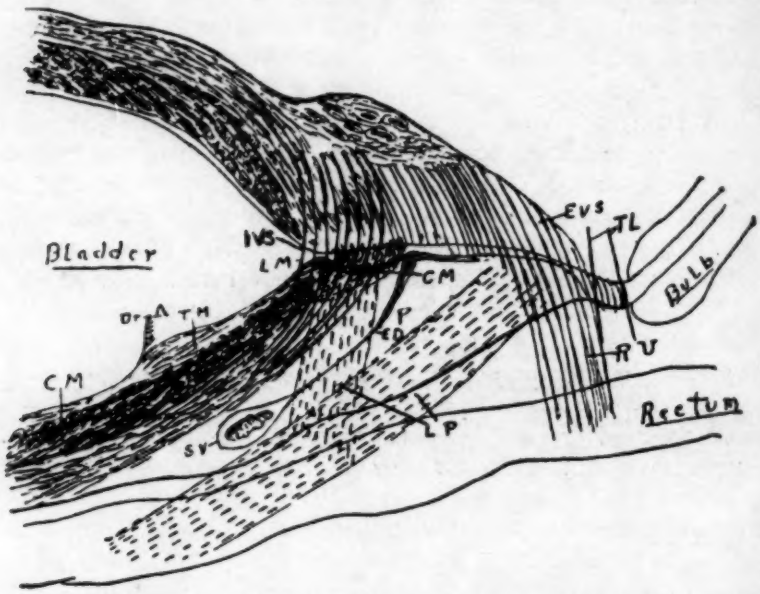

Fig. 3.—Micturition, sphincter closed. Note the angularity existing between the pendulous urethra (at bulb) and the prostatic urethra. *R.U.* indicates the recto-urethralis muscle; *L.P.*, the levator prostatae (striated) muscle (part of the levator ani muscle); *E.V.S.*, the external vesical sphincter (striated); *I.V.S.*, the internal vesical sphincter (nonstriated), with *L.M.*, longitudinal muscle, and *C.M.*, circular muscle; *T.M.*, the trigonal muscle; *P.*, the prostate; *E.D.*, the ejaculatory duct; *S.V.*, the seminal vesicles; *Ur*, the ureter; *T.L.*, the triangular ligament (two layers); *Bladder L.M.*, the longitudinal muscle, and *Bladder C.M.*, the circular muscle. (After Redewill: J. A. M. A. **91**:1960 [Dec. 22] 1928.)

the trigonal muscles is associated with or institutes the contraction of the bladder wall (by the action of the parasympathetic nerves). The external sphincter which is under volitional control then relaxes, and the bladder is emptied. During urination, the striated muscles about the posterior urethra (compressor urethrae, bulbocavernosus and trans-

verse perinei muscles) are in a state of relaxation, for by a voluntary contraction of these muscles the stream can be cut off at will. When the bladder is emptied, the internal sphincter closes and the last portion of urine escaping from the bladder into the urethra in the male is ejected in spurts due to the rhythmic contractions of the compressor urethrae and the bulbocavernosus muscle. Following this, there is a relaxation of the entire voluntary musculature including the external vesical sphincter. The bladder now returns to a state which will permit filling and distention.

Young was the first to emphasize the rôle of the trigone in the mechanism of urination. His original observations on the action of

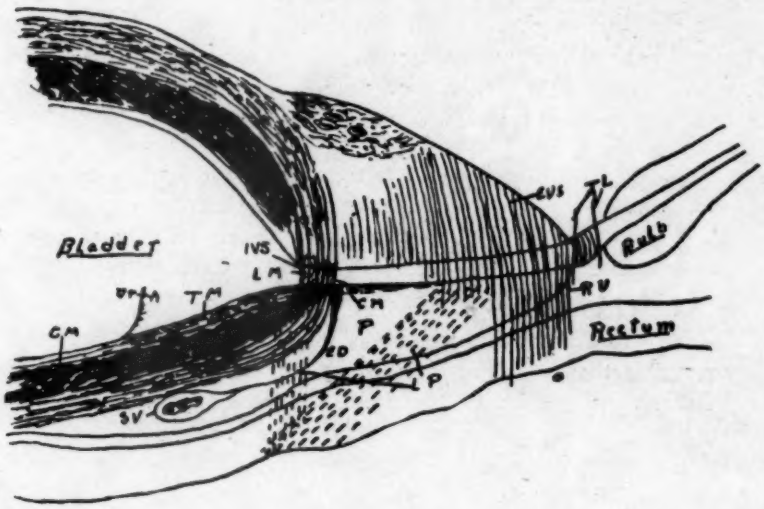

Fig. 4.—Micturition, sphincter open. The nomenclature is the same as in figure 3. Note the angularity of the prostatic urethra reduced with the sphincter relaxed, the urethra becoming almost a straight tube during micturition. (After Redewill: J. A. M. A. **91**:1960 [Dec. 22] 1928.)

the trigonal muscle were made on a patient who had a violent desire to void during a cystoscopic examination. He observed a violent contraction of the trigone and Bell's muscles and a thickening and shortening of the ureteral ridges and Mercier's intra-ureteric bar. He noted that the posterior lip of the vesical orifice flattened out and disappeared due to the contraction of the trigonal muscle which, as has been described before, passes downward over the posterior margin of the vesical orifice into the posterior urethra in the form of an arc. By its contraction, the trigonal muscle pulls down on the internal vesical orifice and opens the sphincter, forming a triangular wide open hole through which the urine may escape. Its contraction also causes a

shortening of the posterior urethra thereby pulling the verumontanum up almost into the bladder. These observations were confirmed by Young and Wesson in their extensive study of the trigone.

Micturition Reflexes.—It is of historical interest to recall the theory of the mechanism of urination advanced by Goetz in 1874. He maintained that distention of the bladder eventually produces a reflex contraction of the bladder walls which squeezes a few drops of urine into the posterior urethra and that the desire to void arose from a stimulation of the sensory nerves of the posterior urethra. This view found support in the fact that stimulation of the posterior urethra by instruments, chemicals or inflammatory reactions causes a desire to void.

The fallacy of this theory is evident when one considers that women have no prostatic urethra and that in many males the prostatic urethra fails to respond to any stimulation. Walker has also pointed out that in cases in which the entire prostatic urethra was removed during a suprapubic prostatectomy there was no appreciable difference in the sensation to void. He also pointed out that in many cases of suprapubic prostatectomy the prostatic urethra became a part of the bladder and naturally held some urine, yet the desire to void came only when the bladder was distended.

In 1882, Mosso and Pellancani studied the volume of the bladder in women with the aid of a catheter, and were the first to show that the desire to void arose from stimulation of the sensory nerves of the bladder. This theory has received general acceptance, and its validity has been subtantiated by the work of the recent contributors to the subject.

The normal voiding reflex is initiated by a conscious sensation of fulness which stimulates the sensory nerves of the bladder. The amount of urine necessary to induce this sensation of desire to void is not constant but varies greatly in the same or different persons. The determining factor is the intravesical pressure rather than the volume of urine in the bladder. The threshold of intravesical pressure is dependent on the degree of irritability manifested by the bladder walls.

Graves and Davidoff have made a comprehensive study of the response of the vesical musculature to normal distention. Their studies reveal that the filling of the bladder is not a passive act but rather a distinct muscle activity as characterized by rhythmic wavelike contractions. These contractions are feeble as filling begins but become more marked as the degree of distention increases. The contractions do not invoke a conscious sensation or desire to void until the upper limits of bladder distention are reached. When the maximal intravesical distention is reached, all rhythmic contractions cease, and there develops a tonic sustained contraction of the bladder walls on its contents. It is at this point that micturition normally takes place. These

authors point out that during the period of gradual filling, the bladder response is immediate and is manifested by an increase in the length of the muscle fibers without materially changing the tension. When the bladder distention approaches the maximal capacity, the response is isometric as the fibers maintain the same length and respond to stretching force (distending fluid) by a rapidly increasing intravesical tension. Thus it is that the intravesical pressure is the controlling factor in urination, for the maximum capacity of the bladder at a given time is solely dependent on the tone of the musculature. Micturition ensues only when the sustained contraction of the bladder wall has attained a certain degree of intravesical tension.

The foregoing facts have been substantiated by Rose in his recent cystometric studies. He noted that as the normal bladder was filled at a constant rate there was a gradual increase in the intravesical pressure to the point of sensation of the first desire to void. At this point, the volume of fluid in the bladder varies from 125 to 175 cc. with an average pressure of from 5 to 15 mm. of mercury. If the filling of the bladder is continued beyond this point, the intravesical pressure arises more rapidly until the patient expels some of the fluid around the catheter, or until the point of normal contractibility of the bladder is overcome, at which time the pressure mounts very rapidly from 40 to 65 mm. of mercury and the patient then complains of severe pain until relieved. It has been frequently observed that a rapid filling of the bladder through a cystoscope or catheter or the use of irritating solutions will induce an imperative desire to void before the desired volume of fluid has been introduced. Likewise, rapid diuresis will cause frequent micturition through a stimulation of the bladder musculature by a smaller amount of fluid than normal.

When the bladder is empty or is undergoing gradual distention, the bladder musculature (detrusor) is in a state of relaxation and the internal sphincter is in a state of tonic contraction controlled by the true sympathetic fibers (hypogastric nerves). As the bladder undergoes complete distention and the intravesical pressure increases, the rhythmic contractions of the bladder walls give rise to afferent impulses which pass chiefly by way of the pelvic nerves to the sacral portion of the cord (and perhaps to a lesser extent by hypogastric nerves to the twelfth thoracic and first lumbar segments) and thence to the higher cranial centers. These afferent impulses are increased as the bladder becomes fully distended, and emptying of the bladder takes place as the result of reflexes set up in the lower sacral cord. These stimulate the sacral parasympathetic fibers of the nervi erigentes supplying the bladder and thus cause a contraction of the bladder wall and a relaxation of the internal sphincter. This reflex emptying of the bladder is accompanied normally by a voluntary effort which is the result of

afferent impulses from the distended bladder reaching the cerebrum and giving rise to the conscious desire to void. They also give rise to efferent impulses which cause a contraction of the abdominal and respiratory muscles, thereby increasing intra-abdominal pressure and aiding in the contraction of the bladder.

The contraction of the abdominal walls, however, is not an essential part of the act of urination, for the emptying of the bladder may be entirely reflex depending solely on the intravesical pressure. When the intravesical pressure reaches from 20 to 30 mm. of mercury, the bladder will contract and force the urine through the vesical orifice and urethra. The reflex emptying of the bladder may be inhibited under certain conditions as the bladder is very sensitive to reflex stimulation of psychogenic or sensory origin, which may produce considerable and continual changes in the size and tension of the bladder. It is well known that stimulation of any sensory peripheral nerve will cause a contraction of the bladder. The thought of voiding, the sound of running water, emotional states (fear, fright, anger, etc.,) may induce a desire to urinate when the bladder contains but little urine. In such instances, if micturition is prevented by a voluntary contraction of the striated muscles about the posterior urethra, the bladder may relax and the attendant sensation of fulness with the desire to void will pass away until the urine accumulates within the bladder to a point where the intravesical pressure causes a normal sensation of fulness and a desire to void. In other instances, urination may occur before the bladder has accumulated enough urine to initiate the emptying reflex, either by voluntary effort or by virtue of sensory impulses originating in the other parts of the body and affecting the spinal center in the same way that impulses from the bladder do.

Other Mechanisms of Urination.—In the foregoing pages, we have described in detail the normal mechanism of urination which results from voluntary effort acting on the spinal centers and reenforced by the contraction of the skeletal muscles. In addition to this mechanism, two other mechanisms will be considered: (1) intrinsic bladder mechanism (as in the Goltz and Ewald dogs), and (2) reflex automatic bladder resulting from visceral afferent and efferent impulses.

Intrinsic Bladder Mechanism: This system of bladder-emptying naturally infers an automatic nervous apparatus confined within the bladder walls, i. e., intrinsic nerve plexus. Von Zeissl (quoted by Kretschmer) was able to isolate completely the bladder of dogs from all nerve connections with the central nervous and autonomic systems and found that after an interval they were able to retain their urine and to urinate. Goltz and Ewald removed the lumbar and sacral segments of the spinal cord in dogs and observed that after a primary but temporary retention of urine the dogs gradually developed an auto-

matic contraction of the bladder and in a few months were able to urinate regularly and periodically. Graves pointed out that such automaticity must be attributed to the inherent properties of the bladder muscle fibers which are most likely controlled by the intrinsic nerve plexuses which exist throughout the vesical musculature. Starling (quoted by Graves) stated that in a bladder severed from its connections with the central nervous system, the automatic rhythmic contractions caused by the accumulation of urine in the bladder gradually increase in force until one of the contractions is able to overcome the resistance of the tonically contracted internal sphincter. Although urination follows in such cases, the bladder is not completely emptied as the intravesical pressure falls rapidly to a level too low to maintain the patency of the internal sphincter. Consequently, there is always some residual urine. The intrinsic automatic bladder may follow a complete transverse lesion of the spinal cord below the level of the twelfth thoracic segment, and clinically, is encountered in cord tumors, injuries of the cord, varicose veins of the cord, degenerative lesions of the cord, local arachnoiditis, etc., where the lumbosacral portion of the cord is involved.

Automatic Reflex Bladder: This type of emptying mechanism is purely involuntary, since it is operated from the cord (fig. 2). There is a complete dissociation of the voluntary portion of the normal emptying mechanism operated from the cerebrum, for as long as cerebral connections with the bladder are intact, an automatic reflex bladder is impossible. Automatic reflex micturition is possible, provided the reflex centers in the spinal cord are preserved and functioning. The automatic reflex bladder is the functional emptying mechanism in infants and is considered a part of the primitive mass reflex system. Following injuries to the spinal cord and disease of the cord above the level of these reflex centers, the bladder is no longer under volitional control. In other words, transverse lesions of the cord below the level of the red nucleus as far down as the level of the twelfth thoracic or first lumbar spinal segments results in the establishment of an automatic reflex bladder and is usually associated with flexor spasms and sweating below the level of the lesion. The amount of urine that the bladder can hold under such conditions varies, but usually is about from 200 to 250 cc. However, this mechanism of automatic emptying of the bladder is dependent mainly on the intrinsic activity of the bladder musculature and frequently proves inefficient due to a maladjustment of the reflex mechanism accompanying the shock of an injury to the spinal cord. In such cases, the urine accumulates until the intravesical pressure is great enough to force open the internal sphincter allowing the urine to dribble out feebly, and as a result the bladder is incompletely emptied and a varying amount of residual urine is left behind as a focus for infection.

It is interesting to note that incomplete transverse lesions (1) of cerebral origin: tumors, cysts, aneurysms, eye strain, strabismus, circumscribed arachnoiditis, etc.; (2) of cerebellar origin: tumor, cysts, hemorrhage, etc.; (3) of vestibular origin: ear and canal lesions; and (4) of spinal origin: tabes, syringomyelia, etc., are never associated with an automatic reflex bladder but may and often do result in incontinence, enuresis and retention. McClintic stated that local organic nerve lesions or irritations may cause a spastic bladder (so-called vagotonia), enuresis and incontinence. Head maintained that irritation of the parasympathetic nerves is the cause of bed-wetting, an incontinence of urine frequently associated with the desire to void; whereas stimulation of the sympathetic nerves causes a paradoxic incontinence (large residual with overflow).

The Rôle of the Internal and External Vesical Sphincters in Maintaining Bladder Closure.—It is of more than passing interest to note the progress of investigation into the normal functions of the vesical sphincters. A review of the literature on the subject reveals many conflicting opinions as evidenced by the fact that at various times the normal control of urination and mechanism of retention of urine has been attributed to either the internal or external vesical sphincter.

The contention that the internal vesical sphincter can volitionally control urination by maintaining bladder closure has now been definitely established by experimental, roentgenologic and operative observations. Rehfisch, in 1897, was the first to prove that the internal sphincter is capable of voluntary contraction. He introduced a metal catheter into the posterior urethra, so that its opening was beyond the external sphincter but not quite up to the internal sphincter, and noted that the patient could control voiding perfectly. Prior to this, Born, by his plaster of paris injections of the bladder in cadavers, and Barkow, Henle and Kohlrausch, by their anatomic studies of the vesical neck, considered the internal sphincter the point of normal closure of the bladder although they differed as to the exact structure of this sphincter.

Further confirmation of the normal function of the internal sphincter in maintaining closure of the bladder was obtained by the roentgenologic studies of Voelcker and Lichtenberg in 1907. They filled the bladder with 5 per cent collargol and showed that the internal sphincter maintained closure of the fully distended bladder, and at the same time they showed that the outline of the normal bladder was pear-shaped, being broad above and narrowed down at the vesical neck. They were unable to show a funnel-shaped formation with obliteration of the internal vesical sphincter when the bladder was fully distended. Other investigators (Leedham-Greene, Barringer and MacKee, Uhle and MacKinney, and Hyman), working along similar lines and using the same or different opaque mediums in the bladder, confirmed these

results. However, one notes a difference of opinion as to the shape of the bladder when fully distended. Barringer and MacKee, and Hyman have confirmed the observations of Voelcker and Lichtenberg, whereas Leedham-Greene and Uhle and MacKinney found the bladder to be oval, approaching a round form. Legueu described a reverse type with the bladder broad at the base and narrow at the fundus as characteristic of the normal patient in prone position. Typical cystograms of normal bladders in our studies can be seen in figure 5.

Further support of the ability of the internal sphincter to maintain bladder closure is found in observations on the mechanism of control of urination following various operative procedures. Young has repeatedly pointed out that in a properly performed perineal prostatectomy in which the triangular ligament, compressor urethrae and external sphincter have been retracted along with the transverse perinei

Fig. 5.—Normal cystograms obtained by injecting from 300 to 350 cc. of 3.5 per cent sodium iodide solution through a soft rubber catheter with the patient in the horizontal position. These cystograms demonstrate the normal point of bladder closure at the internal sphincter in the fully distended bladder. The contour of the bladder approaches a round form.

muscles and in which a small slitlike incision is made into the posterior urethra near the apex of the prostate, it is not uncommon to see the patient regain control of the internal sphincter in a few days. Thus the patient is able to retain his urine within his bladder or to expel it voluntarily from the perineal wound, and in some instances even to close the bladder after part of the urine has been passed. Following an external urethrotomy (for strictures of posterior urethra), wherein the external sphincter is cut or damaged but the internal sphincter is preserved, normal control of urination ensues and incontinence of urine rarely occurs except in those cases of stricture in which the

internal sphincter is destroyed or damaged by the continuous pressure of urine within a chronic distended bladder.

It appears that there is a unanimity of opinion concerning the adequacy of the internal sphincter in controlling bladder closure in the moderately distended bladder, but a marked diversity of opinion exists concerning the mechanism of bladder closure in the fully distended bladder. Earlier writers, Guyon, Ultzman, Finger, Ruggles and Wilson and McGrath, were of the opinion that the internal sphincter was too weak to maintain closure of the bladder under all conditions. They believed that the internal sphincter was sufficient to close the bladder when moderately distended, but under full distention the internal sphincter was overcome and the compressor urethrae, and presumably the external sphincter, were brought into action to retain the urine within the bladder. They contended that there was a funnel-shaped opening formed in the region of the vesical neck owing to distention of the posterior urethra with urine and an obliteration of the internal sphincter. They contended that in the fully distended bladder there is a shortening of the posterior urethra of from 1 to 1.5 cm. more than occurs in the moderately distended bladder. However, this point has been ably refuted by von Zeissl, who has shown that this shortening is not sufficient to account for placing closure at the compressor urethrae or external sphincter which is situated 4 cm. from the vesical neck, and that the latter distance would be the amount of contraction necessary to place the closure at the external sphincter. The beliefs of these earlier workers were substantiated in part by the work of Oppenheim and Loew on monkeys. The latter workers made roentgenographic studies after injecting a bismuth suspension into the bladder and concluded that the compressor urethrae prevented the escape of urine from the fully distended bladder. Their work, however, was not very conclusive, and has not altered the prevailing and accepted theory that the internal sphincter maintains volitional control of bladder closure.

For a long time physiologists have argued against this view, maintaining that such a phenomenon would present the paradoxic example of volitional control of involuntary smooth muscle. That such control may exist is not beyond reason or expectation and finds a counterpart in the volitional control of the muscles of accommodation of the eye. A likely explanation of the volitional control of closure of the bladder by the internal sphincter has been aptly put forth by Cecil on the basis that the contraction of this sphincter is due to a "reflex, voluntarily initiated."

The question of the rôle of the external vesical sphincter in maintaining bladder closure has long been a debatable one. It has been contended that the function of the external sphincter in controlling urination after the internal sphincter has been rendered useless by oper-

ative intervention, or by continuous dilatation from an enlarging prostate. is not the normal function of the external sphincter but merely an abnormal circumstance, the external sphincter having taken upon itself a reflex ability to control urination. In other words, it is nature's method of compensating for a deranged internal sphincter. Nevertheless, it has been definitely established that the external sphincter is capable of maintaining bladder closure by itself, for observations during and following suprapubic and perineal prostatectomies show that when the external sphincter is preserved, perfect bladder closure and urination results regardless of whether or not the internal sphincter is preserved or injured beyond repair. Young and Cecil both have pointed out that often following a perineal prostatectomy the internal sphincter is inactive and there is a continuous drainage from the perineal fistula. When the fistula closes, normal voiding occurs, indicating that the external sphincter has assumed control of urination and bladder closure. Further confirmation of the ability of the external sphincter to maintain bladder closure is found in men with deranged internal sphincters resulting from paralysis from a nerve lesion, for these men do void normally although the posterior urethra may be filled with urine. Roentgenologic studies in animals and men in whom the bladder and vesical neck have been rendered useless by artificial or acquired interference with their nerve supply have also confirmed the ability of the external sphincter to maintain control of urination and the retention of urine. Wallace and Hyman have demonstrated by roentgenograms that the external sphincter was the point of bladder closure after suprapubic prostatectomy.

Perhaps the most conclusive evidence of the ability of the external sphincter to function independently of the internal sphincter has been offered by Young in an experiment supplementing that of Rehfisch. He inserted into the vesical orifice of normal men a metal tube mounted on a curved slender rod, thus rendering the internal sphincter functionless. He noted that the men were able to maintain full closure of the bladder by bringing the external sphincter into action and also were able to start and stop their flow of urine at will.

It seems that under normal circumstances the external sphincter supplements the action of the internal sphincter and that its assistance in maintaining bladder closure while very useful is not absolutely essential.

The preponderance of data obtained tends to show: first, that the normal bladder closure is maintained by the internal vesical sphincter; second, that when the internal sphincter is rendered functionless by operative intervention or from long continuous dilatation and stretching by an intravesical enlargement of the prostate, the external vesical sphincter is capable of maintaining bladder closure; third, that either the

internal or external sphincter can be rendered nonfunctioning and normal urination and bladder closure made to follow, providing the remaining sphincter is in normal condition.

THE PATHOLOGY OF INCONTINENCE

The pathology of urinary incontinence following prostatectomy is still in its inceptive stage, although recently a considerable amount of new information has been obtained through the studies of Wade, Hyman, Cecil, Watson, Herman, Walker, Gordon and Denslow. There still exists an imperfect understanding of the readjustment of the musculature of the vesical neck following operative intervention.

It is interesting to note the various explanations for incontinence following prostatectomy that have been offered in the past. In 1901, Woolsey, in discussing three cases of incontinence following perineal prostatectomy reported by Parker Syms, said that incontinence may be partly explained by the injury to the fibers of the prostatic urethra and faulty healing subsequent to the operation. In 1903, Lilienthal explained incontinence on the basis of changes in healing at the neck of the bladder and urethra. He believed that a soft succulent scar at the neck of the bladder and posterior urethra was inducive to a continent bladder, but that a hardened cicatrized scar in this area would lead to a rigid urethra with incontinence. Moore, in 1904, stated that incontinence following prostatectomy is due to injury to the muscles or the nerves or to the neck of the bladder, most often the latter. He also stated that an injury to that "portion of the sphincter of the bladder just below the urethra and in front of the third lobe" (external sphincter?) during operation may result in incontinence. In 1905, Ballenger and Ruggles independently stressed the necessity of avoiding injury to the external sphincter during prostatectomy. Ruggles stated that the derangement of the external sphincter may be due either to an injury to the nerve supply of the external sphincter or to the sphincter itself during the manipulations incidental to removal of the prostatic enlargement especially in the perineal prostatectomy. He wisely suggested that in a perineal prostatectomy the incision into the urethra should be made as close to the prostate as possible and urged extreme caution to avaid stretching and laceration of these muscles.

In 1911, Proust, in writing of the complications of perineal prostatectomy, stated that the mechanism of incontinence is extremely difficult to understand. He pointed out that the vesical neck is not the cause for two reasons: First, the hypertrophied prostate causes an excentric dilatation of the internal vesical sphincter with eventual destruction; and second, incontinence never occurs after a suprapubic operation where manipulation is confined to the vesical neck and the prostatic urethra. He maintained that incontinence following perineal

prostatectomy is due either to a direct lesion of the membranous urethra or to an injury to its nerve innervation. He expressed the belief that the occurence of incontinence following perineal prostatectomy is due to the trauma incidental to a difficult operation in removing a very large or firm prostate.

Judd, in 1911, expressed the belief that both the internal and the external sphincter play some part in the control of urine after prostatectomy. He stated that in a perineal prostatectomy it is important to preserve the prostatic capsule, especially in the region of the neck of the bladder, and not to save the elongated and distorted prostatic urethra.

Gardner believed that the preservation of the compressor urethrae muscle following suprapubic or perineal prostatectomy insures a good funtional result. He attributed postoperative incontinence to the difficulty associated with the removal of a prostatic obstruction wherein the hyperplastic masses were not easily enucleated. He stated that in such cases injury or partial removal of the aforementioned muscle occurred, and maintained that the injury or removal of the internal sphincter does not have any effect on actual muscular control of urination.

Young (1922), in his article dealing with the operative cure of incontinence, stressed the pathologic structural changes associated with postoperative incontinence following median urethrotomy, perineal and suprapubic prostatectomy. He mentioned the following operative defects: (*a*) a wide dilatation of both the internal and external sphincters, with incontinence due to lack of function of the external sphincter; (*b*) wide dilatation of the membranous urethra due to division of the external sphincter posteriorly; (*c*) postoperative scar tissue in the perineum, and (*d*) widely dilated internal sphincter with absence of the usual elevation of the median portion and with scar tissue replacing the muscle in that region.

Changes that occur at the vesical neck in cases of incontinence following prostatectomy must necessarily be determined by a study of the surgical pathology of this region. Such a study engrosses the observations recorded at the time of the operation, or after operation with the aid of the cystoscope, urethroscope and x-rays, or at autopsy after operation. Before undertaking a study of the changes associated with incontinence, it is fitting to discuss the structural changes that normally occur after suprapubic and perineal prostatectomy. Walker, Young, Hinman, and Watson have made important contributions to this phase of the subject, and we have drawn frequent references from their work.

Changes Following the Suprapubic Method.—In the vast majority of cases, the readjustment of the musculature about the vesical neck

following this method is manifested by the development of a structural defect, i. e., a cavity formation. The presence of such cavity formation was first noted by Walker in 1904 (quoted by Wallace in 1907), and later clearly demonstrated roentgenographically by Wallace and Page in 1911 and by Hyman in 1914. This cavity is essentially a dilatation of the prostatic urethra following the enucleation of a hypertrophied prostate and results in the prostatic urethra becoming a part of the bladder cavity. The cavity is usually funnel-shaped and quite large, and is accompanied by a widely dilated and functionless internal sphincter. In a few cases the cavity assumes a spindle shape, is not quite as large as in the previous type and is associated with a contracted vesical neck. In the vast majority of cases, the point of bladder closure is at the external sphincter with perfect urinary control as shown by Wallace,

Fig. 6.—Cystogram in case following suprapubic prostatectomy with excellent functional result. The anatomic defect in the form of an enucleation cavity is clearly defined. Perfect bladder closure is maintained by the external sphincter. This is the type of postoperative cystogram found in the majority of cases of suprapubic prostatectomy.

Hyman and others (fig. 6). It is rare to find the internal sphincter restored and functioning after suprapubic prostatectomy, for the internal sphincter is practically always destroyed or rendered useless by the trauma incidental to this method of enucleation. Examination of the bladder cavity at varying intervals after operation reveals a persistently relaxed internal sphincter. In figure 7, a cystogram following a suprapubic prostatectomy in one of our cases is shown. The point of bladder closure appears to be at the internal sphincter, but when closely examined, it is noted that some dye leaks into the enucleation cavity. Perfect closure is thus maintained by the external sphincter. In this case, the internal sphincter was only partially injured

at the time of operation and hence there is a partial restoration of function of this sphincter after operation.

The development of a cavity following suprapubic prostatectomy is dependent on two factors: (1) anatomic changes produced by the enucleation of the prostate and (2) method of packing for controlling hemorrhage. In the hands of the ordinary suprapubic surgeon, the enucleation is essentially a blind procedure with division and injury to the internal sphincter. Since the prostate is normally an extra-vesical and extra-urethral organ, subcapsular enucleation necessarily requires a division of the internal sphincter before the enlarged mass can be shelled out. In removing the hypertrophied tissue, particularly the portion that pushes up under the base of the bladder, the mucous membrane of the bladder about the vesical neck together with the

Fig. 7.—Cystogram in a case following suprapubic prostatectomy in which no incontinence was present. The point of bladder closure is observed at the internal sphincter, except for a small amount of dye which leaked into the enucleation cavity. Absolute bladder closure is maintained by the external sphincter.

dilated internal sphincter is stripped back for some distance. In many instances, complete divulsion of the prostatic urethra is produced unintentionally and leaves a large denuded gap between the bladder and anterior urethra. The manipulation of the finger in the posterior urethra and within the prostatic capsule may cause a varying amount of damage to the intrinsic musculature of the prostatic urethra. The latter musculature when preserved after operation may play an important part in assisting the preserved external sphincter to maintain perfect bladder closure after suprapubic prostatectomy. These anatomic changes aid in altering the shape of the prostatic urethra and bladder by producing a temporary loss of tonicity of the musculature about the vesical neck and by delaying healing of the structural defect about

the prostatic urethra which results from operation and which causes a break in continuity between the bladder and anterior urethra.

To control hemorrhage in the suprapubic operation, the prostatic bed is packed very tightly from above either with gauze or a rubber (Pilcher) bag or a smooth metal cone. Thus the prostatic urethra is dilated and elongated and tends to produce a marked separation of vesical neck from the enucleation cavity. Such a cavity would naturally be exaggerated should repacking be required.

Nevertheless, the existence of a cavity does not interfere with or prevent perfect urination, provided the integrity of the external vesical sphincter is preserved. When a disturbance of urination, such as retention or incontinence, does occur after suprapubic prostatectomy, it is practically always due to permanent injury to the external sphincter or to some mechanical intervention with the function of this sphincter or the internal sphincter in the form of loose fragments of prostatic, urethral or bladder tissue producing a ball-valve obstruction, or to a narrowing of the lumen of the vesicoprostatic orifice produced by stricture, bar or canopy formation. However, the occurrence of such unfavorable structural defects within the enucleation cavity has been greatly decreased by the recent advances in the technic of the suprapubic operation whereby the uncertainty of blind enucleation with the finger has been replaced by accurate dissection in a clearly visualized operative field. Hemorrhage at the time of operation has been controlled more completely by ligation of bleeding vessels and by suturing the torn prostatic capsule and vesical wall than by trusting to the uncertainty of gauze packs.

Changes Following the Perineal Method.—Watson studied the mechanism of bladder closure following perineal prostatectomy and pointed out that there is an early readjustment of the musculature about the vesical neck. The point of bladder closure in practically every instance is found to be at its normal site, i. e., the internal vesical sphincter. The external sphincter should be preserved in every instance following a properly performed perineal prostatectomy. The restoration of function in the internal sphincter may take place as early as three days after operation as manifested by the ability of some patients to maintain bladder closure with perfect urinary continence for one or two hour intervals. The return of function to the internal sphincter is usually complete by three weeks after operation and persists throughout life.

In figure 8 are shown cystograms taken before and after perineal prostatectomy. In the preoperative cystogram (*Pre-O.*), the point of bladder closure is at the internal vesical sphincter. Intravesical bulging of the prostate and a small diverticulum are also shown in this picture. In the postoperative cystogram (*P. O.*), the bladder has assumed an

oval outline with some of the dye leaking into the enucleation cavity. The point of bladder closure is at the external sphincter. These cystograms are the usual ones found in a continent bladder following a perineal prostatectomy where some damage to the internal sphincter occurs at operation but the external sphincter is preserved.

There is usually no cavity formation following a properly performed perineal prostatectomy where the internal sphincter is preserved, but other anatomic and structural changes about the vesical neck may occur which may cause some interference with urination. It is generally conceded that incomplete and irregular enucleation of the prostatic mass, especially in cases with subtrigonal involvement, is more likely to occur after the perineal method than after the suprapubic method. In some cases, the obstruction to passage of urine may be due to loose portions of prostatic tissue and prostatic capsule left behind after incomplete enucleation of the prostate; in other cases,

Fig. 8.—Preoperative (*Pre-O.*) and postoperative (*P. O.*) cystograms in a case of perineal prostatectomy with a continent bladder. The point of bladder closure is at the internal sphincter in the postoperative cystogram. In the latter picture, partial closure is noted at the internal sphincter with some dye in the enucleation cavity. This may be explained by partial injury to the internal sphincter at the time of operation.

deep fissure formation in the posterior urethra or plication of redundant urethral walls may follow the removal of a large adenomatous prostate with marked intra-urethral bulging.

When incontinence does follow a perineal operation, it is always accompanied by some injury to the sphincteric musculature about the vesical neck and posterior urethra. Such a complication should not occur as frequently as it does, for the perineal removal of an enlarged prostate is essentially an extra-urethral and extravesical operation wherein the hypertrophied mass is shelled out of its capsule, leaving both vesical sphincters intact. However, in the hands of an inexperienced surgeon, some damage may be done to the vesical sphincters and to the intrinsic musculature of the posterior urethra in carrying out a

perineal dissection. Injury to the external vesical sphincter can be avoided by making the external urethrotomy incision (for the introduction of the Young's prostatic tractor) at a point below the external sphincter, preferably near the apex of the prostate. This potential danger may also be obviated by omitting the introduction of the Young's prostatic tractor through an incision of the membranous urethra and using a long prostatic tractor which is passed through the external meatus of urethra into the bladder as advocated by Geraghty, Cecil and Morrissey. Unquestionably, prolonged traction on the prostate with such instruments can also damage the internal sphincter. Traction with the Young prostatic tractor should be in an upward and outward direction to avoid further lengthening of the urethrotomy incision anteriorly with subsequent injury to the external sphincter.

As the field of operation in a perineal prostatectomy is constantly under control of the eye, a careful dissection of the perineum can always be carried out, minimizing the traumatization and derangement of the musculature about the vesical neck. The absence of cavity formation after the perineal operation may be attributed to the method of packing the enucleation cavity to control hemorrhage. Hemostasis in the perineal operation is dependent on an intraprostatic compression which is maintained by packing the prostatic cavity lightly with gauze from below, in contradistinction to the suprapubic method of controling hemorrhage by an intra-urethral compression of prostatic cavity from above with subsequent pouchlike dilatation of the enucleation cavity. In the perineal method, the gauze packing within the prostatic cavity is always extra-urethral and tends to compress and obliterate the enucleation cavity. Recently, Young has adopted the use of a Davis rubber bag inserted into the bladder for drainage and hemostasis, and the principles of its hemostatic action are essentially the same as suprapubic method of intra-urethral compression of the enucleation cavity. It is possible for the cavity formation to occur after such a procedure.

Recently the authors have advocated a new technic for perineal prostatectomy in which gauze packs are placed in the prostatic bed between the prostatic capsule and urethral wall for hemostasis only. These are placed against an indwelling catheter placed in the bladder by way of the urethra. The catheter is used for urinary drainage during the convalescence, avoiding the perineal drainage.

By this method the cavity formation mentioned, which is usually formed in the other methods of prostatectomy, is here avoided. We believe that this cavity formation tends to damage or to distort the internal vesical sphincter in a certain percentage of the cases if it is not already damaged during the removal of the prostate.

CAUSATIVE FACTORS OF INCONTINENCE

It matters little which method of prostatectomy has been used, the incontinence of urine resulting from such an operation in every instance is due to a loss of function of both sphincters. As has been previously stated, either the internal or the external sphincter is capable of maintaining excellent control of urination in the event of the loss of function of the other.

The usual operative defect associated with incontinence is a wide dilatation of both the internal and the external sphincter, accompanied by a dilatation of the membranous and posterior urethra. The muscular components of the internal and the external sphincter are replaced by scar tissue. In the region of the internal sphincter, the usual prominence of the median portion is absent, due to the replacement of the injured muscles by scar tissue.

Our investigation, as well as the observations of others, of the vesical neck and posterior urethra in cases of urinary incontinence following prostatectomy reveals various types of anatomic defects or pathologic lesions associated with the loss of function of the internal and external sphincters. These associated changes about the vesical neck or posterior urethra per se do not cause urinary incontinence but may increase the urinary difficulties as a result of the altered urinary passage and hence may be considered as contributory factors. These changes or defects do occur in a large percentage of the cases, and for all practical purposes may be divided into intrinsic and extrinsic groups. In the intrinsic group, which comprises by far the largest number of cases, the anatomic defects associated with urinary incontinence are the result of some structural change at the vesical neck or posterior urethra following operation. The extrinsic group is composed of a very small number of cases in which the urinary disturbance is due to some preexisting lesion or anatomic change in structure which persists after operation and interferes with the proper function of the internal and external sphincters. We wish to stress the fact that the occurrence of many of these anatomic or pathologic changes of either the intrinsic or the extrinsic group, in the presence of one or both good functioning sphincters, has a tendency to produce an obstruction to urination with a resultant retention rather than urinary incontinence. Our studies justify the following classification:

Urinary Incontinence Following Prostatectomy

Etiology

Temporary or Permanent Derangement of the Internal and External Vesical Sphincter

Associated Changes or Contributory Factors

Intrinsic Group

Loose Tissue Flaps at the New Vesical Orifice
- (*a*) Strips of Mucous Membrane of the Bladder
- (*b*) Nodules of Prostatic Tissue
- (*c*) Strips of Prostatic Capsule
- (*d*) Strips of Urethral Wall
- (*e*) Plication of the Urethral Wall

Strictures or Contractions at the Vesicoprostatic Orifice
- (*a*) Canopy Formation
- (*b*) Bar or Ledge Formation

Stricture in the Region of the External Sphincter

Deep Fissure or Sulcus Formation in the Posterior Urethra

Complete Divulsion of the Prostatic Urethra

Extrinsic Group

Hypertrophy of the Trigone

Intravesical or Prostatic Tumors

Vesical Calculi

Atony of the Bladder: Preexisting Nerve Lesions Involving the Mechanism of Urination

Diverticulum of the Bladder

Urethral Lesions (Stricture, Calculi and Tumor)

A brief discussion of the rôle of each factor in the development of postoperative urinary incontinence is in order.

ETIOLOGY

Temporary or Permanent Derangement to the Internal and External Vesical Sphincters.—Many authorities, particularly Walker in writing on the suprapubic and Young on the perineal method, have repeatedly stressed the absolute necessity of preserving the integrity of the vesical sphincters at the time of operation. Their reasons are obvious, since the internal and external vesical sphincters play the most important part in the mechanism of urination and in the maintenance of perfect bladder closure. In many instances, the internal sphincter has already been rendered functionless by the enlarging prostatic adenoma before the patient seeks relief by operative intervention.

The pathologic anatomy of the benign hypertrophied prostate is such that as a rule the adenoma is found on the floor and sides of the posterior urethra. As these adenomatous areas continue to enlarge, the posterior urethra lengthens and the internal vesical sphincter is gradually dilated and stretched, especially as the growth pushes through into the lumen of the bladder. Very often the internal sphincter surrounds and grasps this enlarging adenomatous mass (so-called median lobe hypertrophy) about the waist or central portion so that the upper part of the enlarged gland comes to lie free in the bladder in front of the trigone, presenting the well known intravesical bulging. In many

cases, the portion of the adenomatous gland below the constricting internal sphincter may bulge inward, thus narrowing the lumen of the prostatic urethra and producing the intra-urethral bulging so commonly observed. In the majority of cases, the internal sphincter is temporarily deranged and perhaps in a few cases permanently destroyed when such a condition exists at the time of operation. Consequently, the operator is required to exercise caution to preserve the remaining functioning sphincter (i. e., external sphincter) to insure a good result and to avoid that dreaded bugbear, incontinence.

The proponents of the suprapubic prostatectomy assume that in those cases in which the hypertrophied prostate is removed without wounding the dilated internal sphincter, this sphincter will eventually regain its tone. The question arises: Is the hypertrophied prostate capable of being removed by the suprapubic method without injury to the internal sphincter at some stage of its enucleation? This seems well nigh impossible when one recalls that the prostate is an extravesical organ and that removal by the transvesical approach necessitates a further stretching of an already dilated internal sphincter and division with possible destruction of the internal sphincter. The fact remains, however, that the probability of damaging the external sphincter during a suprapubic enucleation is remote, for the field of operation is confined to an area above the triangular ligament. Hence, one is insured of at least one good functioning sphincter with an ultimate good operative result from the standpoint of urinary continence, for it has been definitely established by Wallace, Hyman and others that the external sphincter is sufficient and does maintain perfect bladder closure after suprapubic prostatectomy.

Young has repeatedly pointed out that injury to either vesical sphincter should never occur during a carefully performed perineal prostatectomy, which calls for (1) retraction of the triangular ligament, external sphincter and transverse perinei muscles; (2) an extra-urethral removal of the hypertrophied gland leaving the internal sphincter and most of the posterior urethra intact, and (3) introduction of Young's prostatic tractor through an incision made below the external sphincter preferably at a point near the apex of the prostate. Nevertheless, there always remains the potential danger of injuring the internal sphincter by prolonged traction with the Young tractor or damaging the fibers of the external sphincter and compressor urethrae muscle in carrying out a dissection of the perineum. It is in the hands of the inexperienced surgeon not fully acquainted with the operative details and technic of the procedure that many of the disparaging cases of incontinence have occurred and perhaps accounts for the unpopularity of this method.

ASSOCIATED CHANGES OR CONTRIBUTORY FACTORS: INTRINSIC GROUP

Loose Tissue Flaps or Tags About the New Vesical Orifice.—Examination of the prostatic cavity after operation often reveals loose masses of tissue (fig. 9) in or about the vesicoprostatic orifice which may interfere with urination. The examiner frequently is at a loss to explain the presence of these loose masses following what he believes to be a perfect enucleation. This type of structural defect is seen most frequently after the suprapubic method. Thomson Walker has written extensively of this type of lesion, and owing to his persistent and untiring efforts, genito-urinary surgeons have become better acquainted with its signs, symptoms and treatment.

Total subcapsular enucleation of the gland by sharp and blunt dissection is practically impossible, and consequently loose fragments of

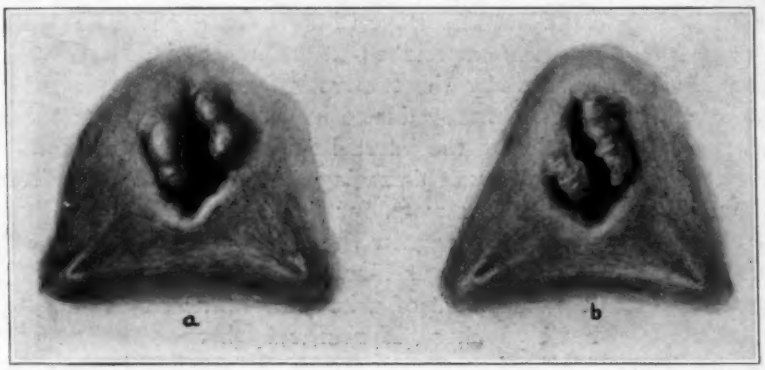

Fig. 9.—Anatomic defects at vesical orifice following suprapubic prostatectomy: *a*, nodules of prostatic tissue at the prostatovesical orifice; *b*, strips or tags of mucous membrane at the prostatovesical orifice. (Drawing after Walker: Brit. J. Surg. **7**:530, 1920.)

prostatic capsule and small nodules of the prostatic adenoma may be left behind, especially if a blind operation is performed. These loose strips of capsule and small nodules of gland tissue are usually loosely attached to the wall of the prostatic cavity and, as a rule, slough away; but occasionally they persist and encroach on the new vesical opening, causing a ball valve or polyp-like obstruction which permits a small amount of urine to escape through the contracted orifice.

The presence of loose flaps of mucous membrane of the bladder is not infrequently encountered. After suprapubic enucleation of the adenoma, the prostatic bed contracts practically at once, but often not quite enough to close entirely the opening between the bladder and the anterior urethra; consequently, there may be left behind on the posterior surface of the bladder one or more unsupported crescent-shaped flaps

of bladder wall with a raw edge and with the dilated internal sphincter attached thereto. This defect is found mainly in those cases in which the adenomatous mass has extended up under the trigone. It is rare to find a loose anterior flap of bladder wall even in those exceptional cases in which there is an enlargement of the anterior lobe. These loose flaps of bladder wall may interfere with urination by acting as a mechanical irritant or by meeting over the prostatic cavity and blocking the newly formed vesicoprostatic opening, causing a permanent or intermittent obstruction. Often these loose flaps may slough away and effect a spontaneous cure, or they may become impregnated with urinary salts and give rise to hard calcareous masses or in some instances to bladder calculi. These loose tags also act as a nidus for harmful bacteria

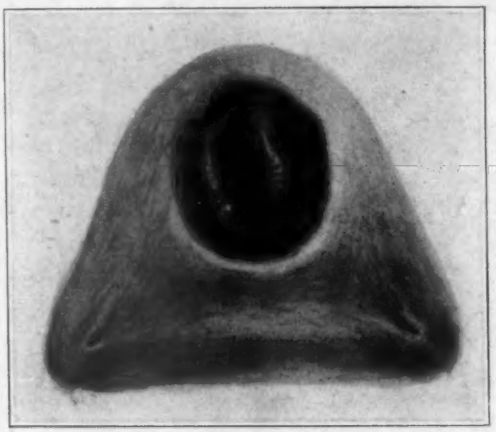

Fig. 10.—Loose strips of urethral mucous membrane or prostatic capsule in the enucleation cavity. (Drawing after Walker: Brit. J. Surg. **7**:534, 1920.)

and serve as a causative or stimulative agent for a persistent post-operative cystitis.

Long loose strips of the posterior urethra wall (fig. 10) coursing the length of the prostatic bed or strips torn across in a transverse direction may occur after the removal of a prostate. They are the results of the tugging and pulling incidental to blind enucleation by the supra-pubic method. Such a defect is likely to follow the removal of a hard fibrous prostate.

Mucosal plications may be present and may lead to interference with urination and obstruction to instrumentation. This type of defect is seen most frequently after the perineal operation in cases of large hypertrophied prostate with marked intra-urethral bulging. In these cases the adenomatous tissue is removed extra-urethrally, leaving redundant hypertrophied walls of the urethra free to sag and meet in the

lumen of the posterior urethra, forming a valvular depression (fig. 10) and thus interfering with proper emptying of the bladder.

Stricture or Contractions at the Vesicoprostatic Orifice.—Canopy Formation (Figs. 11 and 12): This type of anatomic defect occurs most frequently following suprapubic prostatectomy, and may occasionally be associated with urinary incontinence. Thomson Walker has pointed out that stricture formation after prostatectomy is likely to occur at the vesical neck and at the membranous urethra where the mucous membrane of each is severed or torn across during the process of enucleation. The most frequent site for the occurrence of stricture or stenosis is at vesicoprostatic margin. Here the edges of the torn bladder

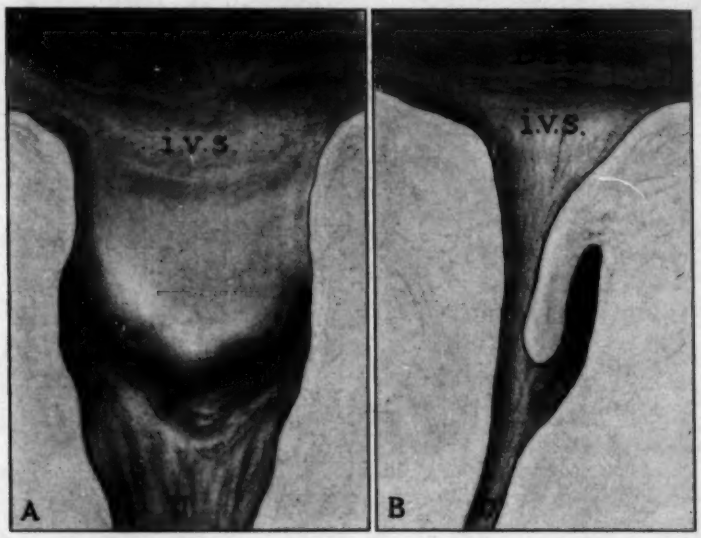

Fig. 11.—Redundant posterior urethral wall forming a valvular depression in a case of incontinence observed by the authors. This patient had a perineal prostatectomy performed at another hospital. *A* shows the posterior view; *B*, the sagittal view; *Bl* indicates the bladder; *i. v. s.*, the internal vesical sphincter; *U*, the posterior urethra.

mucosa posteriorly and laterally tend to grow together and form a canopy or tympanum which shuts off the prostatic cavity from the bladder. In those cases in which the hypertrophied prostate is removed by intra-urethral manipulation without completely injuring the dilated internal sphincter, the sphincter may regain its tone within a week, and as the contraction progresses, the sphincter is drawn together in the manner of a purse string, narrowing the vesical outlet.

It appears that in the majority of cases the internal sphincter will normally contract more readily than the remainder of the enucleation

cavity and regain its tone quickly as the component circular fibers of the injured or weakened sphincter gather strength. It is in the rare case that the degree of contraction of the internal sphincter is marked, so that the resultant vesicoprostatic opening becomes narrowed and often sclerosed by the increasing amount of fibrous components of the internal sphincter which occurs during the process of healing.

If one were to inspect the bladder in a case with canopy formation, one would find the vesical orifice presenting itself either as a small opening, a dimple or a bud of granulation tissue located well forward near the anterior wall of the bladder. As a rule, the anterior lip of the opening is represented by a very slight ledge where the bladder wall

Fig. 12.—Canopy formation over enucleation cavity following suprapubic prostatectomy as a result of union of the lateral folds: *a*, view from the bladder; *b*, sagittal section. (Drawing after Walker: Brit. J. Surg. **7**:529, 1920.)

becomes continuous with the urethral wall. The posterior lip is formed by a hard, fibrous, crescent or sickle-shaped fold. The formation of this diaphragm is dependent on the drawing up of the lower segment of the bladder by contraction of the internal sphincter, thus preventing a natural coalescence of the mucous membrane of the bladder and anterior urethra within the enucleation cavity.

On passing a sound or catheter through the urethra in such cases, one experiences great difficulty in finding the opening on the tympanum, even with the aid of a finger in the bladder. One is easily misled to believe that the instrument is in the bladder, whereas it is merely

pushing up on the tympanum like a tent pole. As Gordon has pointed out, the enucleation cavity beneath the canopy is often large enough to permit the complete rotation of a short beaked sound within it. The difficulty in introducing the instrument may be attributed to a failure of the posterior urethra to serve as a guide because of the misalinement of the posterior urethra with the opening in the tympanum.

The incidence of such canopy formation is fortunately rare. Its relative infrequency is perhaps due to the fact that in most cases the internal sphincter has been sufficiently injured at the time of operation and its healing delayed long enough to permit a natural coalescence of the mucosa of the bladder and anterior urethra.

Bar or Ledge Formation (Fig. 13): In some cases of urinary incontinence following prostatectomy, more so after the suprapubic than

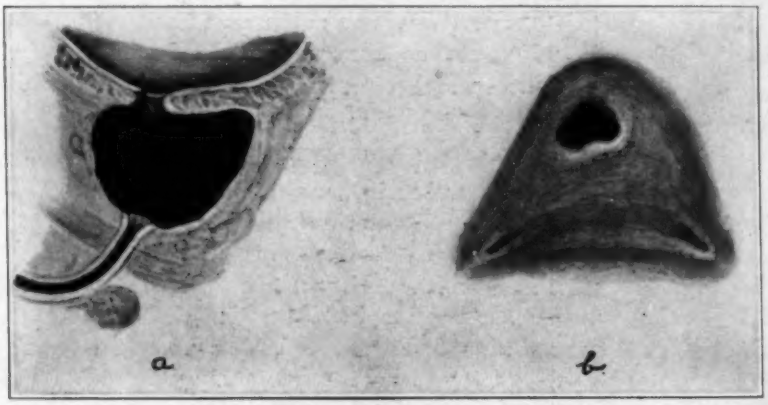

Fig. 13.—Canopy formation at prostatovesical orifice resulting in unusual healing of posterior wall of bladder. The opening into the bladder is situated at the anterior aspect of enucleation cavity. *a* shows the sagittal section; *b*, the view from the bladder. (Drawing after Walker: Brit. J. Surg. **7**:529, 1920.)

after the perineal method, there may be found at the posterior lip of the vesicoprostatic orifice either a transverse bar or a raised crescent-shaped ledge which tends to narrow the lumen of the opening and interferes with the emptying of the bladder. This bar or ledge is formed by the trigone and parts of the continuous posterolateral walls of the bladder plus a part of loosely attached internal sphincter. The formation of this type of defect is due to the trauma incidental to the enucleation of a large intra-urethral prostate with subtrigonal enlargement.

Stricture in the Region of the External Sphincter.—Stricture formation at the anterior end of the prostatic bed with resultant marked dilatation of the prostatic bed and bladder is theoretically possible, but actually rare. Such a complication should never occur after a supra-

pubic prostatectomy, but could follow a perineal operation when the external sphincter is injured through faulty dissection or from undue traction with the prostatic tractor.

Deep Fissure or Sulcus Formation in the Posterior Urethra.—In some cases of urinary incontinence following prostatectomy, there is occasionally found a deep sulcus or fissure in the floor of the posterior urethra, extending from the internal sphincter to the bulb, which interferes with the action of both sphincters. Occasionally the sulcus or depression may take a transverse course across the urethra, especially on the posterior urethral wall (fig. 14). This type of lesion occurs most

Fig. 14.—Ledge formation within the posterior urethra due to redundant urethral walls; small nodule of tissue projection on the posterior surface of urethra. This patient was operated on at another hospital and developed complete incontinence. *Tr.* indicates the trigone muscle; *i. v. s.*, the internal vesical sphincter; *p. u.*, the posterior urethra.

frequently after perineal prostatectomy and perineal operations for strictures of the urethra following gonorrhea, and is due to the trauma and delayed healing following an incision of the posterior urethra. It is possible that in some cases of perineal prostatectomy the traction on the Young prostatic tractor may cause a further gaping of the incision in the posterior urethra. It is also possible that the use of a Davis rubber bag or a rubber tube inserted into the bladder for hemostasis or drainage purposes may produce an exaggerated separation of the fibers

of the prostatic urethra and may lead to delayed healing with ultimate fissure or sulcus formation.

Complete Divulsion of the Prostatic Urethra.—It is commonly believed that the entire prostatic urethra is removed in the suprapubic operation for an intra-urethral hypertrophied prostate, while in one that bulges intravesically the enucleation may be performed without the entire removal of the prostatic urethra. However, such a defect may occur not only during suprapubic prostatectomies but also during perineal prostatectomy when the prostate is removed "en masse." In the majority of cases of this type, the torn edges of the mucosa of the bladder and anterior urethra successfully bridge the gap within a short time and heal without interference with urination. In a very few cases in which the entire circumference of the posterior urethra has been removed, stricture formation has resulted which required postoperative dilatation or another operation to remove the obstruction to urination. Careless removal of the prostate en masse by either method of postatectomy may cause irreparable damage to both sphincters with resulting incontinence.

EXTRINSIC GROUP

Hypertrophy of the Trigone.—In view of the rôle the trigone normally plays in opening the vesical orifice during micturition, it is not surprising to find a compensatory hypertrophy of the trigone when there is an obstruction of the vesical orifice by an enlarged median lobe. Occasionally, the hypertrophied trigone is seen through the cystoscope as a distinct enlargement behind the vesical neck, but most frequently the hypertrophied trigone forms a firm compact mass with the enlarged prostate. Young pointed out that when the obstruction (hypertrophied prostate) is removed there is often an associated atrophy or diminution in size of the enlarged trigone. As early as 1911, Young stressed the fact that a true hypertrophy of the trigone may exist without an enlarged prostate and present signs of obstruction to urination by acting as a transverse dam in the floor of the bladder. In long-standing cases, the hypertrophied trigone produces a pouchlike depression (bas fond), and the latter undermines the trigone and dissects it free from the bladder causing a valvelike obstruction to urination. Such an obstruction might easily be overlooked at operation, and its persistence after operation may interfere with the passage of urine. Thomson Walker was the first to emphasize the rôle that the thickened walls of the trigone played in the formation of ledge or canopy obstructions following suprapubic prostatectomy, and he strongly advised the precautionary measure of removing at the time of operation a wedge-shaped portion of the posterior vesicoprostatic septum as far as its junction with the bladder.

Intravesical or Prostatic Tumors.—Preexisting papilloma of the bladder may also serve as a valvelike obstruction to urination after operation, and in rare instances may cause an incontinence of an infiltration of the tissue near the vesical neck, thus interfering with the action of the internal sphincter. Occasionally, a nodule or lobe of adenomatous tissue may be left behind at the time of operation, and this may continue to grow and cause some interference with urination.

Another cause of postoperative incontinence is the recurrence or further growth of a carcinoma of the prostate which may not be suspected at the time of operation.

Vesical Calculi.—Vesical calculi occurring shortly after operation are usually due to the impregnation of loose flaps of bladder or prostatic tissue with the mineral salts of the urine. They usually lead to some degree of ball-valve obstruction at the newly formed vesical orifice and result more often in retention than in incontinence. The calculi may be found in either the bladder or the prostatic pouch but rarely in both. Occasionally, small calculi will be found in the shallow cellules or between trabeculations.

Atony of the Bladder.—Atony of the bladder walls due to a prostatic obstruction may cause a false incontinence in the sense of an overflow or retention in the nonoperative case. Removal of the hypertrophied prostates in patients with a marked degree of atony may be followed by a temporary and usually partial incontinence. It is generally agreed that atony of the bladder dependent on a prostatic obstruction and incident to old age is not a contraindication to operation, provided the entire obstruction is removed at operation. Incomplete restoration of the tone of the bladder musculature and a small amount of residual urine may follow the complete removal of the prostate in many of the cases.

It is essential to differentiate preoperatively the type of atony of the bladder associated with the prostatic obstruction from the nonobstructive type produced by diseases of the central nervous system. Tabes and cerebrospinal syphilis are the most common causes of the nonobstructive type of bladder atony, and less frequent causes are tumor of the spinal cord or injury, lateral or multiple sclerosis and syringomyelia. The retention that follows a cerebral or spinal lesion may be partial or complete, depending on the degree of atony of the bladder walls, and the incontinence that often follows is dependent on the degree of paralysis of the internal and external vesical sphincters. Consequently, all cases of atony of the bladder should be carefully differentiated before operation by cystoscopic, complete neurologic and serologic studies; otherwise patients with hopeless cases will be submitted to an operation with absolutely no chance for a good functional result. Although the prostate is atrophied as a rule in the presence of a spinal lesion, in rare instances a true hypertrophy may exist. In such cases, if the spinal lesion is not

too far advanced and the atony of the bladder is definitely proved to be due to the prostatic enlargement, operative intervention with removal of the obstruction is warranted.

Diverticulum of the Bladder.—A diverticulum of large or moderate size may act as an obstruction to the escape of urine from the bladder and urethra. This type of lesion must be considered in those patients in whom a complete routine study (including cystoscopy and cystography) was not made for any of various reasons.

Urethral Lesions.—The presence of a stricture of the anterior or the membranous urethra, calculi in tumors of the urethra, may possibly serve as a cause of postoperative urinary discomfort, but fortunately such lesions are readily detected preoperatively and successful treatment can be readily instituted.

REPORT OF CASES

CASE 1.—C. H. S., aged 64, was admitted to the Sinai Hospital on Jan. 13, 1927, with a history of marked diurnal and nocturnal frequency. He stated that he had had a sensation of not completely emptying his bladder after voiding. Rectal examination revealed no enlargement of the prostate. On cystoscopic examination, it was noted that there was 100 cc. of residual urine with a capacity of 400 cc. There was only slight bulging of the prostate laterally, but a rather marked median lobe was present. There was practically no intra-urethral bulging. Many cellules and trabeculations were observed. The urine showed a 2 plus sugar reaction.

On February 11, when the urine was free from sugar as the result of diabetic treatment, a one-stage suprapubic prostatectomy was performed. The lateral lobes were fibrotic and difficult to remove. The median lobe was the largest of all and was also fibrotic.

There was delayed healing of the wound, but finally it closed. At the time of discharge from the hospital, the patient was able to void in a good stream and was able to start and stop the stream, but there was some dribbling between and at the end of urination. Treatment was given for this, but no relief was obtained. Six months after the operation, cystoscopic examination revealed marked relaxation of the posterior segment of the vesical orifice. The posterior edge appeared to be drawn up to the ureteral orifices, indicating marked relaxation of the internal vesical sphincter. There appeared to be a small diverticulum in the posterior urethra, just behind the verumontanum.

A cystogram (fig. 15), taken after the injection of 630 cc. of 3.5 per cent sodium iodide, revealed the point of closure to be at the internal vesical sphincter with some dye leaking through the internal sphincter.

A urethrogram, taken after the injection of 20 cc. of 3.5 per cent sodium iodide into the posterior urethra, revealed a slight irregularity but no definite pouch formation.

Comment.—Partial urinary incontinence in this suprapubic case is the only one in our series, although its occurrence is not infrequent with other surgeons. The explanation is simple, and its occurrence has been of tremendous value to us, for we feel that in our cases it will not occur again in the near future under similar circumstances.

In this case, the bladder had been drained with a catheter for several weeks prior to operation. The history of urinary difficulties plus the amount of residual urine served as the reason for a prostatectomy. At operation, a very small fibrous prostate was found with very slight bulging laterally and a very small median lobe. It was quite a task to remove the fibrous growth from its capsule, and in the manipulations incidental to its removal it is extremely likely that fibers of both sphincters were torn, resulting in incontinence. We believe that the logical procedure in a case of this type in the future is a punch operation performed without opening the bladder or at the operating table when an examination reveals a small fibrous gland.

Fig. 15.—Cystogram in a case of partial incontinence following suprapubic prostatectomy. The point of bladder closure was at the internal sphincter, but some dye escaped through both sphincters.

Case 2.—S. S., aged 61, was admitted to Sinai Hospital on May 10, 1926. He had the usual symptoms of prostatic enlargement, consisting of diurnal and nocturnal frequency, hesitancy, urgency and dribbling. He had acute urinary retention on several occasions. Rectal examination revealed a very large right lobe with a smaller left one, of a soft and doughy consistency, with no evidence of malignancy. Cystoscopic examination revealed the amount of residual urine to be 60 cc., with a bladder capacity of 300 cc. There was marked intravesical and intra-urethral bulging of the prostate on the right, less marked on the left, with a moderate amount of bulging posteriorly in the form of a median lobe.

On October 29, perineal prostatectomy was performed. The bulb was unnecessarily exposed and an incision was made high in the membranous urethra. The lateral incisions were made in the prostatic capsule and then connected, making it an inverted "U" incision. The prostate was removed en masse, taking the prostatic urethra with it. A catheter was passed into the bladder by way of the

urethra and another into his bladder by way of the external urethrotomy incision. One iodoform gauze pack was placed in each prostatic cavity.

On his discharge from the hospital, four weeks after operation, his perineal wound was closed. He was voiding in a good stream, every one to one and one-half hours during the day and about every two and one-half hours during the night. There was some dribbling between urination and at the end of urination. Under treatment, this improved somewhat but not entirely. Eleven months after operation a cystoscopic examination was made, and this revealed several small pouchlike areas in the posterior urethra with several irregularities, giving one the impression that the musculature near the external sphincter had been injured.

On Jan. 22, 1929, which was twenty-seven months after the operation, a cystogram was taken with the patient in both the horizontal and the erect postures. These revealed the outline of the bladder to be oval, after 200 cc. of 3.5 per cent sodium iodide was injected. There was no leakage into the posterior urethra when the patient was in the horizontal position (fig. 16). When he was erect,

Fig. 16.—Cystogram taken with the patient in the horizontal position in a case of partial incontinence following perineal prostatectomy. The bladder outline appears normal with the point of bladder closure at the internal sphincter. No dye can be seen escaping through the internal or the external sphincter, but in the upright position a few drops did leak past both sphincters.

it was observed that there was some leakage into the urethra and a few drops passed out through the external meatus. His condition, however, was improved. He could retain his urine at times as long as one and one-half hours without dribbling. Most of the dribbling was done in the afternoon. He could stop and start the stream in an excellent manner, but did have some dribbling between urination.

Comment.—The resultant urinary incontinence in this case is of the partial type. Despite the fact that the patient is able to start and stop his stream voluntarily, he suffers from the inconvenience of wearing a small receptacle to catch the drippings when any sudden movement is made. There is a loss of from 1 to 3 ounces of urine during the day but none at night.

The persistence of diurnal dribbling implies that both vesical sphincters have been damaged to some extent. The derangement of the sphincters though relatively slight is permanent notwithstanding the ability of the patient to start and stop his stream. The damage to the external sphincter undoubtedly occurred when the urethrotomy incision for the insertion of the prostatic tractor was made high in the membranous urethra rather than close to the apex of the prostate. A contributory factor may be the faulty traction on the prostatic tractor in an upward direction which tends to split the external sphincter in the line of the urethrotomy incision. The injury to the internal sphincter most likely occurred when the prostatic adenoma was removed en masse. A more careful enucleation of the prostate from around the vesical orifice probably would have obviated some injury to the internal sphincter. However, we are inclined to believe that had we made the urethrotomy incision for the prostatic tractor at the apex of the prostate (as we do today), the external sphincter, the preservation of which is of paramount importance, would not have been injured and no incontinence would have resulted. In a careful dissection of the perineum in a perineal prostatectomy, the bulbous urethra and external sphincter should never be exposed.

Case 3.—J. A., aged 66, was admitted to the Sinai Hospital on June 20, 1928, in uremic coma. A history obtained from the patient on examination two years prior to admission was that he had urinary difficulty, such as urgency and diurnal and nocturnal frequency. A rectal and cystoscopic examination revealed a benign prostatic adenoma of the third degree. Owing to his condition of uremic coma, he was considered a very poor operative risk. Nevertheless, after fluids were forced and a retention catheter used, the patient's condition improved so much that on July 27 a perineal prostatectomy was performed, caudal anesthesia being used. Two lateral incisions were made in the prostatic capsule, and the lobes were removed separately. The median lobe was delivered into one of the lateral openings. The prostatic bridge of tissue was preserved, likewise the prostatic urethra, except for a small tear in the urethra which was made when the median lobe was delivered. The internal sphincter seemed undisturbed and was not unusually dilated; hence it was dilated with an instrument at the completion of the operation. The external sphincter was retracted up during the operation. Packs were placed in the capsule pressing against a urethral catheter which was inserted into the urethra, at the time of operation.

The catheter was removed on the fifteenth postoperative day, and the patient began voiding in a good stream, but he also dribbled between urination and at the end of urination. This was also noted when the patient would suddenly arise from a sitting posture. No nocturnal dribbling was present.

A cystogram (fig. 17), taken on Feb. 5, 1929, revealed a well outlined bladder with an imperfect closure at the internal sphincter. Some of the dye (3.5 per cent sodium iodide) leaked into the posterior urethra and out past the external meatus.

When the patient was last seen on April 4, 1929, the dribbling was still present.

Comment.—This case illustrates the type of partial incontinence that may develop following a perineal prostatectomy. The causative factors of the incontinence are not quite clear, but undoubtedly both vesical sphincters were damaged during the operation.

The injury to the external sphincter was probably due to a faulty incision in the membranous urethra and may have been aggravated by the prolonged traction of the prostatic tractor. The damage to the internal sphincter is less easily explained since the prostatic adenoma was enucleated in separate portions, preserving the integrity of the posterior prostatic capsule and leaving the prostatic urethra intact except

Fig. 17.—Cystogram in a case of partial incontinence following perineal prostatectomy. Imperfect bladder closure at the internal sphincter is noted. Some dye leaked into the posterior and anterior urethra.

for a small tear. At the completion of the operation, the internal sphincter appeared to be of good tone, and instrumental dilatation of this sphincter was performed as usual, which may have injured the sphincter. However, it is conceivable that the internal sphincter was temporarily or permanently destroyed prior to operation by the dilatation accompanying the increased growth of the adenoma.

This patient also had a very large direct inguinal hernia on the right side occupying the entire scrotal sac. It was present before and after the operation, and the patient refused operative treatment. While a large hernia may occasionally interfere with urination, especially when

there is an accompanying herniation of the bladder, we are inclined to believe that the presence of the hernia did not influence the production of the persistence of the urinary incontinence, as cystographic and cystoscopic studies failed to reveal any bladder defect directly associated with the hernia.

CASE 4.—B. L., aged 59, was admitted to Sinai Hospital on Sept. 17, 1928, with symptoms of prostatic enlargement. Cystoscopic examination revealed a large intravesical bulging of the median lobe and a moderate intravesical and intra-urethral bulging of both lateral lobes. A diagnosis of benign prostatic adenoma of the second degree was made. The patient appeared to be a good surgical risk.

On October 5, perineal prostatectomy was performed with the patient under caudal anesthesia. An incision was made in the membranous urethra, close to the apex of the prostate for the insertion of the Young prostatic tractor. An inverted "U" incision was made in the capsule, and the prostate was removed en masse. The urethra was not preserved, but the prostatic capsule was. The prostate was of the adenomatous and fibrous type. At the completion of the operation, the internal sphincter appeared to be dilated. The external sphincter was retracted up with the transverse perinei muscles during the operation. A catheter was inserted into the bladder, and gauze packs were placed in the capsule against the catheter. The catheter was removed on the eighteenth day, and the patient began voiding, with some diurnal incontinence and terminal dribbling. As time went on, he began to get better control of urination. He could stop and start the stream, but he has never had perfect control. The patient was last seen on March 11, 1929, five months after the operation, and he had only partial control of the stream during the day. Dribbling was present between and at the end of urination. Dribbling also occurred while he was walking or sitting, and especially if he stood up suddenly. His stream was of good force.

A cystogram (fig. 18), taken three months after operation, revealed partial closure of the bladder at the internal sphincter with some dye leaking into the posterior urethra. No dye escaped through the external sphincter which maintains bladder closure.

Comment.—This case illustrates partial incontinence following perineal prostatectomy. The patient is able to pass urine in a good stream at fairly regular intervals. He is able to start the stream with ease, but there is some dribbling at the end of and between urination. Thus, at five months after operation, complete control of urination is lacking.

In this case, the incision in the urethra for the prostatic tractor was not made close to the apex of the prostate but rather high in the membranous urethra, with possible injury to the external sphincter. Misdirected traction of the prostate by the prostatic tractor may also have caused some injury to this sphincter. The prostatic enlargement was removed en masse, taking with it the prostatic urethra and probably tearing some of the fibers of the internal sphincter. The injury to both sphincters could not have been complete, otherwise the patient would have had no control of urination.

Case 5.—W. N., aged 76, was admitted to the Sinai Hospital on Nov. 29, 1918, with symptoms of prostatic enlargement. The usual examinations were made, including examination of the urine, blood, rectal, cystoscopic and roentgenographic studies. After a careful study, a diagnosis of benign prostatic adenoma of the third degree was made. The patient was considered a poor operative risk. The cystoscopic study, which is of importance in connection with this paper, revealed marked intra-urethral and intravesical bulging of the prostate. As the patient's general condition was very poor, the bladder was drained with a retention catheter for over three and a half months. After considerable difficulty and a long period of time, his general condition improved, and a perineal prostatectomy was performed on March 18, 1919. Some of the details of the operation in this case were as follows: (*a*) two lateral incisions were made in the prostatic capsule through which one very large lateral lobe and the other very large lateral and moderate-sized median lobe combined were removed, and (*b*) the incision in the urethra for the tractor was made in the membranous portion above the apex of the prostate.

Fig. 18.—Cystogram in a case of partial incontinence following perineal prostatectomy. The bladder outline is normal. Partial bladder closure is noted at the internal sphincter with some dye leaking into the posterior urethra. No dye escaped through the external sphincter which maintains bladder closure.

At the completion of the operation, the internal sphincter seemed to be undisturbed and to have a fairly good tone. The urethra was partly injured during the removal of the median lobe. The external sphincter was thought likewise to be uninjured, but no particular observation of injury was made at the time. After closure of the perineal wound, which occurred on the nineteenth day, difficulty in urination was noted in that straining on urination and dribbling was present. Attempts were made to dilate the urethra, but these failed.

A diagnosis of urethral deformity or urethral stricture was made. On April 19, an external urethrotomy was performed. On May 2, the patient was discharged from the hospital, voiding in a good stream but with slight dribbling at the end of and between urination.

After his discharge on May 2, he had diurnal and nocturnal incontinence, and on Aug. 29, 1919, he was again admitted to the hospital for further observation. Cystoscopic examination at this time revealed a slight bulging at the right and

left anterolateral aspects of the vesical orifice, where two small lobulations were observed hanging down from the vesical orifice. There was marked relaxation of the posterior urethra. A perineal operation was performed on October 15, at which time repair of the external sphincter was attempted. A redundant membranous urethra was found, and plastic repair was performed for the formation of a new external sphincter. A catheter was inserted into the urethra. A stricture again resulted from this operation.

On Jan. 19, 1920, he was again admitted to the hospital and dilatation was done with a filiform and followers. On one of these occasions, a filiform broke

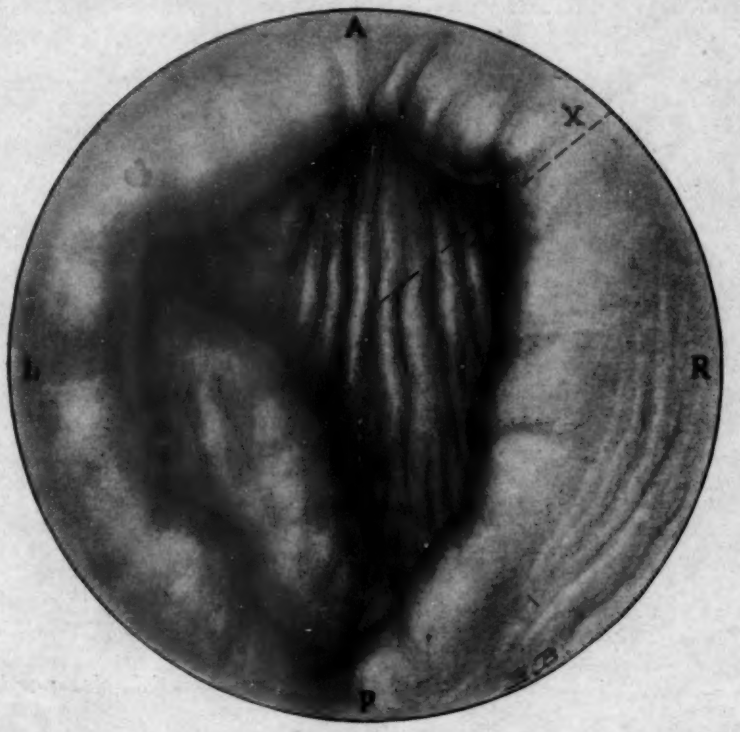

Fig. 19.—Relaxed and redundant posterior urethral walls with a bar of urethral tissue in a case of complete urinary incontinence following perineal prostatectomy in the authors' series. This patient also had a stricture in the posterior urethra about 2 cm. from the vesical orifice which is not shown in the drawing. *X* indicates posterior wall of urethra. *A* indicates anterior; *P*, posterior; *R*, right; *L*, left.

off in the bladder, and an external urethrotomy was performed on February 18. The patient was discharged from the hospital on March 6. Complete urinary incontinence was present following these various operations. On March 1, 1921, he was again admitted for observation, but was discharged on March 5. The last time the patient was heard from was six months after his last discharge from the hospital, at which time he still had incontinence.

CASE 6.—B. M., aged 59, was admitted to the Sinai Hospital with only mild symptoms of prostatic hypertrophy. Examination revealed an enlargement of the first degree in a man who was a good operative risk. Cystoscopic study revealed a few small calculi in his bladder. There was very slight bulging of the prostate laterally, but a moderate-sized median lobe was present.

A perineal prostatectomy was performed on Dec. 16, 1927, with the patient under nitrous oxide anesthesia. A urinary obstruction developed after the perineal prostatectomy. The perineal fistula failed to close. At each act of urination all the urine drained through the perineal fistula, none passing through the urethral canal. The attempt to urinate caused the patient excruciating pain, owing to the inability of the urine to pass through the contracted internal sphincter. A stricture of the internal sphincter was diagnosed.

Fig. 20.—Cystogram in a case of complete incontinence following a perineal prostatectomy. The bladder outline is cone-shaped with cavity formation in the posterior urethra due to loss of function of the internal sphincter and to the presence of a stricture in the posterior urethra. Incompetency of the external sphincter is illustrated by the escape of dye into the anterior urethra.

On Jan. 4, 1928, a plastic repair of the vesical neck was performed by the suprapubic route. At the operation, the internal orifice seemed somewhat dilated, but in the region of the old prostatic urethra was found a flap of tissue which appeared to obstruct completely the outflow of urine (fig. 19). Attempts to pass a sound beyond this obstruction through the urethra or retrograde from the bladder were unsuccessful. This was finally broken through. The urethra was then dilated and a catheter inserted. After the removal of the catheter urinary incontinence still existed, but urine came through the urethra with ease. The perineal wound was closed. Stricture of the posterior urethra developed shortly after operation, which necessitated another operation. A suprapubic cystotomy

with retrograde catheterization was performed on January 27, with little relief from the urinary difficulty.

Urinary incontinence continued for one year. On Feb. 12, 1929, plastic repair of the vesical orifice was attempted. No operation was performed on the membranous urethra at this time. The result was a failure as the urinary incontinence persisted. A bar was observed across the internal orifice. This was excised in the hope of relief.

When last seen, the patient had complete urinary incontinence. A further plastic operation is to be considered.

A cystogram (fig. 20), taken after the prostatectomy, demonstrates a cone-shaped bladder with definite cavity formation up to the point of stricture in the posterior urethra. The dye has leaked past this strictured area into the anterior

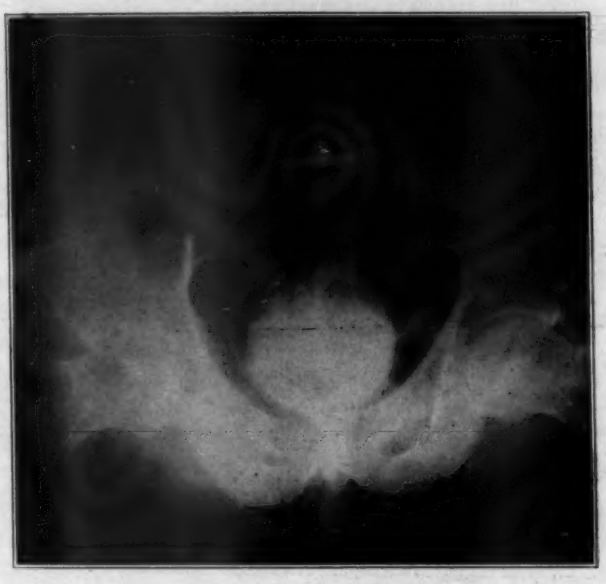

Fig. 21.—Cystogram in a case of complete incontinence with the dye completely filling the anterior and posterior urethra, indicating total loss of function of the internal and external sphincters.

urethra. This cystogram illustrates the complete loss of function of both sphincters.

Comment.—Cases 5 and 6 illustrate the occurrence of complete urinary incontinence following perineal prostatectomy. The etiologic factors and resulting anatomic defects appear to be the same in both cases.

Following the perineal prostatectomy, a stricture resulted which caused the incontinence. Despite repeated dilatations of the stricture and a secondary operation on it, the incontinence persisted.

In both cases, the stricture occurred between the membranous urethra and the vesical orifice, about 1 or 2 cm. from the vesical orifice. The

vesical orifice was patent and dilated in each case, but an obstruction to the passage of a sound was encountered just before the sound reached the vesical orifice. In addition, there was an obstructing bar in one case (B. M., fig. 19), which deflected the tip of the sound.

In both cases, the urethrotomy incision for the insertion of the Young prostatic tractor was made high in the membranous urethra rather than close to the apex of the prostate. This procedure undoubtedly injures the external sphincter. The internal sphincter, which is the sphincter most frequently injured in either a perineal or a suprapubic prostatectomy, was destroyed here by the tugging and trauma incidental to the removal of an adenomatous and fibrous gland intimately surrounding the internal sphincter.

Two cases of complete urinary incontinence came under our observation after perineal prostatectomy had been performed at another institution. Both patients had complete incontinence. In both cases, cystoscopic study revealed a markedly dilated internal sphincter and relaxed external sphincter. In one case (fig. 14), there was a redundant flap of the posterior urethra, and in the other case (fig. 13) there was a redundancy and relaxation of the posterior urethral walls resulting in ledge formation in addition to a small lobulation of tissue on the posterior urethral wall. A cystogram in the latter case (fig. 21) shows complete loss of bladder closure due to incompetent internal and external sphincters.

TREATMENT

Many operative procedures have been described for the treatment of postoperative urinary incontinence in the male. The methods vary from a plastic operation on both vesical sphincters through the combined suprapubic and perineal routes to the transplantation of a voluntary muscle (i. e., the levator ani, rectus abdominalis, pyramidalis, etc.) about the neck of the bladder or urethra. We have attempted many of these methods in the treatment of postoperative urinary incontinence with varying degrees of success. A discussion of our experiences and results with these methods will be presented in a separate article to be published in the near future.

CONCLUSION

1. Urinary incontinence following suprapubic or perineal prostatectomy occurs more frequently than one would suspect after a thorough review of the literature.

2. In our series of 220 prostatectomies, postoperative urinary incontinence of some degree occurred in 1 case (0.7 per cent) of 134 suprapubic and 5 cases (5.8 per cent) of 86 perineal prostatectomies.

3. Urinary incontinence occurs more frequently following perineal than suprapubic prostatectomy.

4. Urinary incontinence indicates a lack of complete control of the passage of urine through the urethra. The degree of incontinence may be complete or partial, depending on the degree of control of urination manifested.

5. Urinary incontinence may follow any suprapubic or perineal operation when both vesical sphincters are involved.

6. The occurrence of urinary incontinence following either type of prostatectomy is dependent on the destruction or derangement of both vesical sphincters.

7. The failure to preserve either the internal or external vesical sphincter will result in urinary incontinence.

8. In the hands of experienced surgeons, the probability of damaging either vesical sphincter is decidedly less during a perineal than during a suprapubic prostatectomy.

9. It appears that in the majority of cases the functioning sphincter following suprapubic and perineal prostatectomy is the external vesical sphincter, but in some cases of perineal prostatectomy the internal sphincter may also be preserved.

10. In our studies of prostatectomy we found that the etiologic factor in the production of urinary incontinence is more frequently injury during operation to the external sphincter than injury to the internal sphincter, as the internal sphincter may have been injured or destroyed prior to operation.

11. The type of hemostasis employed may influence the preservation or destruction of one or both sphincters.

12. Hemostasis in the suprapubic prostatectomy is essentially an intra-urethral compression of the enucleation cavity from above by means of gauze packs or hemostatic bags or metal cones. The same condition exists when a Davis bag is used for hemostasis in a perineal prostatectomy. Such a method tends to form a pouchlike deformity in the posterior urethra and to dilate further and possibly destroy the internal vesical sphincter.

13. Hemostasis when the perineal method is used is dependent on an intraprostatic compression maintained by packing the prostatic cavity (between the preserved urethral wall and the prostatic capsule) from below with gauze. In this manner, damage to the vesical sphincters is avoided.

14. Injury to the vesical sphincters can be avoided in a properly performed perineal prostatectomy: (1) by retracting the external sphincter and transverse perinei muscles upward; (2) by making the urethrotomy incision for the introduction of the Young prostatic tractor below the external sphincter, preferably at or near the apex of the

prostate; (3) by an extra-urethral removal of the hypertrophied gland, leaving the internal sphincter and prostatic urethra intact, and (4) by exerting traction on the Young prostatic tractor in an upward and outward direction.

15. The introduction of a catheter into the bladder through the urethra at the completion of a perineal prostatectomy facilitates the healing of an injured vesical sphincter and acts as a splint to preserve the continuity of the urethral walls.

16. Various anatomic defects about the vesical neck and posterior urethra resulting from suprapubic and perineal prostatectomy may be associated with the loss of function of both vesical sphincters.

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ACTINOMYCOSIS OF THE THORAX*

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The cases of actinomycosis of the thorax have been divided into two groups: primary and secondary. Actinomycosis of the thorax is considered primary when the infection involves some organ or tissue within the thorax, primarily. Secondary actinomycosis of the thorax is a condition in which the organs or tissues of the thoracic cavity become involved secondarily to an actinomycotic lesion elsewhere in the body.

Clinically, Naussac[1] classified actinomycosis of the lung as: (1) broncho-actinomycosis, (2) pneumo-actinomycosis and (3) pleuro-pneumo-actinomycosis. Choux[2] added a fourth group, thoracopulmonary actinomycosis, to designate the involvement of the thoracic wall.

In primary actinomycosis of the thorax, infection may take place by inhalation of the organism or by infection of the esophagus, from which the mediastinum, pleura and lung become involved. The lungs may be involved secondarily, by direct extension, by embolic or metastatic means, or in the manner in which primary actinomycosis is acquired, presumably as a result of the lesion in the body.

The manner in which the disease is acquired makes little difference in the ultimate outcome, as observed at necropsy. At postmortem examination of patients who have died of actinomycosis of the thorax, one frequently finds over the affected side one or more hard, indurated, bluish-red, boardlike swellings in which a draining sinus or several draining sinuses may be present. The most common sites of these actinomycotic abscesses are: anteriorly, near the breast or in the axillary region, and posteriorly, near the angle of the scapula. If the tissue over one of these abscesses is incised, a fistulous tract which extends into the diseased pleura frequently may be found. When the ribs in such a region are exposed, occasionally elevation of the periosteum and some erosion of the rib will be found. When the thoracic cavity is opened,

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1. Naussac, Joseph: The Pathology, Symptomatology, and Differential Diagnosis of Pulmonary Actinomycosis, Internat. Clin. **3**:1, 1921.

2. Choux, quoted by Naussac (footnote 1).

a thick, fibrous pleura is encountered which is densely adherent to the thoracic wall by thick, fibrous bands, forming a meshwork in which small or large amounts of pus may be harbored. Numerous, irregular canals may be found coursing through the thickened pleura. The canals may lead to an abscess or to a bronchus.

The lung may present two types of lesions. In one type, the lung is large, edematous, heavy and leathery; this is known as the pneumonic type because, on section, the appearance frequently is that of disseminated hepatization. Small, firm, grayish-yellow nodules frequently are found scattered through the pneumonic area. If section is made through one of these nodules, it stands out above the surrounding tissue, and frequently a small amount of liquid material may escape from it. Careful examination of this material usually reveals the presence of a tiny, grayish-yellow granule, the sulphur granule. The surface of such a lung is usually irregular and rough as a result of broken adhesions. In the other type of lesion, the lung is small, sclerotic, and retracted toward the hilum. The surface of the lung is smooth.

TABLE 1.—*Summary of Symptoms in Forty Cases of Primary Actinomycosis of the Thorax Recorded in the Literature*

Symptoms	Present	Not Recorded	Absent	Doubtful
Fever	34	1	1	4
Cough	36	1	..	3
Pain	38	2	..	..
Expectoration	27	4	4	5
Hemoptysis*	3	5	17	5
External abscess	32	2	6	..
Sinuses	23	8	9	..
Loss of weight†	30	5	2	2
Involvement of ribs	10	10	9	11
Involvement of vertebrae	4	..	..	..
Involvement of sternum	1	..	..	..
Anemia	20	6	2	10

* In ten cases the sputum was streaked with blood.
† One patient gained weight.

The bronchial tree may show few changes. There is peribronchial fibrosis and, possibly, slight thickening and edema of the walls. The lumen may be irregularly dilated, and at times a bronchus may be completely plugged with mucoid material.

Microscopically, the disease is characterized by marked hyperplasia of the interstitial connective tissue, large areas of granulation tissue, abscesses, integrity of the blood vessels and absence of giant cells.

PRIMARY LESIONS

This study is based on thirteen cases of primary actinomycosis of the thorax observed at the Mayo Clinic. The condition was also found in forty cases reported in the literature, and the significant symptoms were tabulated (table 1) with a view of correlating the conditions in the two series.

Age and Sex Incidence.—In the series of cases observed at the clinic, eleven patients were males and two, females. The average age was 34 years. In the forty cases from the literature, twenty-seven of the patients were males and thirteen, females, a ratio of 2:1. The average age was 28 years in both sexes. The youngest patient suffering from the disease was a child, aged 2½ years, and the eldest, a man, aged 65 years.

Site of Election.—The side first affected was so predominantly the right in the present series of cases that I was surprised to find that several authors had stated that the left side was the one of election. This difference of opinion caused me to undertake an accurate study of the data from forty cases reported in the literature, with special reference to this point. Of the forty cases, the right lung was involved primarily in twenty, while the left lung was involved primarily in only fourteen; in five cases it was questionable whether the disease began in

TABLE 2.—*Site of Involvement in Primary Lesions*

	Right Lung	Left Lung	Right and Left Lungs	Right or Left Lung ?	Mediastinum	Not Given
Forty cases from literature	20	14	..	5	..	1
West	8	17	2	..	..	..
Mayo Clinic	9	2	..	1	1	..
Total	37	33	2	6	1	1

the right or in the left lung, and in one case the side involved was not mentioned. In West's [3] series, the lung primarily involved was the left in seventeen cases, the right in eight cases, and both lungs were involved primarily in two cases. In the series here reported, the right lung was involved primarily in nine cases; the left lung was involved primarily in two cases, the mediastinum in one case, and in one case, the side primarily involved was questionable (table 2).

From this review, it appears that the right lung is involved more frequently than the left. The site of election in the lung depends to some extent on the mode of infection. On account of the more vertical direction of the bronchus to the lower part of the right lung, inhaled foreign particles are more likely to go to this lobe. It is reasonable to conclude that the lower lobe of the right lung would be more frequently affected when actinomycosis is contracted by inhalation. If the lung becomes involved by means of the second source of infection, the

3. West, Samuel: Case of Primary Actinomycosis of the Pleura, in a Child of Six, with a Table and Analysis of Recorded Cases of Primary Actinomycosis of the Lung and Pleura, Tr. Path. Soc. London **48**:17, 1897.

esophagus, then by virtue of its anatomic position one would expect the left lung to be the seat of the disease more frequently than the right.

According to Cope,[4] the lower lobe is affected twice as frequently as the upper lobe. In West's series, the lower lobe was involved in thirteen cases; the upper lobe, in three cases, and the middle lobe in four cases.

Symptoms.—The patient dates the onset of his illness, in many instances, from the time a blow was received on the chest or shortly thereafter. Whether or not the impact is sufficient to create an injury or place of lowered resistance in the mucosa of the bronchial tubes or the esophagus is doubtful. However, such a history is sufficiently common to be noteworthy.

The clinical sypmtoms of actinomycosis of the thorax may simulate those of two or three other diseases. The type of disease that the condition simulates, depends both on the mode of infection and on the extent to which the disease has progressed when the patient comes under observation.

If the organism is inhaled, the first tissue to react is the bronchial mucosa. The reaction may be so limited that there will be no objective symptoms, and the organisms will pass immediately through the bronchial wall to involve the pulmonary parenchyma. On the other hand, there may be rather diffuse stimulation of the mucous-forming cells of the bronchial tubes, giving rise to profuse expectoration, varying in character from almost pure mucous to fetid mucopurulent viscous sputum in which there are greenish-gray or yellowish-gray bodies. The symptoms are suggestive of simple catarrhal or mucous bronchitis when the sputum is mucoid, and bronchiectasis when the sputum is fetid. The typical sulphur granules may be found in the sputum at this time. Rarely, as in Canali's [5] case, the disease is confined to the bronchial tree. It may be said, therefore, that in the bronchial form the symptoms of actinomycosis are those of mucous bronchitis, occasionally accompanied by cough and usually associated with productive expectoration which may or may not be fetid, in which on careful, repeated examinations of the sputum, *Actinomyces* may be found.

In some cases the organisms spread from the bronchus through the bronchial wall to involve the pulmonary tissue. In a few of these cases, although involvement of the lung is widespread, there may be no symptoms indicative of organic trouble until late in the course of the disease.

4. Cope, V. Z.: A Clinical Study of Actinomycosis with Illustrative Cases, Brit. J. Surg. **3**:55, 1915.

5. Canali, quoted by Hektoen, Ludvig: Actinomycosis of the Respiratory Tract, Internat. Clin. **2**:97, 1901.

Frequently, however, the disease spreads rapidly along the bronchial tubes and bronchioles and produces, with the aid of secondary organisms, bronchopneumonia. In this event, the patient will have fever, cough, pain, malaise, and other toxic symptoms, and the sputum may possibly be blood-tinged. The general and roentgenoscopic observations, too, are those of bronchopneumonia. The disease runs the course of ordinary bronchopneumonia with the exception that the symptoms do not subside as quickly as would be expected in a case of simple pneumonia. After four or five weeks, the patient notes definite loss of strength and possibly some loss of weight, which, in conjunction with the history of cough and, at times, of blood-tinged sputum, lead the physician to suspect tuberculosis. In uncomplicated cases, repeated examinations of the sputum will be negative for bacilli of tuberculosis. At this stage, a correct diagnosis is not often made and, consequently, the patient is treated for tuberculosis. In the course of time, the disease spreads peripherally to involve the pleura, and gives rise to the symptoms encountered in the pleuropulmonary form; the symptoms will be commented on under this heading.

In other cases, the symptoms may be solely those of an abscess, which may rupture into a bronchus and cause a quantity of pus to be expectorated. The associated fever and toxic symptoms are relieved thereby. On the other hand, the abscess may remain practically stationary, or may find a path to the pleura, eventually causing empyema. Roentgenoscopic examination of the thorax frequently will show the presence of an abscess.

In most cases, general examination shows the lesion in the lower lobe. Roentgenologic examination shows peribronchial infiltration, with a rather marked degree of pulmonary fibrosis; if abscesses are present these frequently will be visible.

When the disease has progressed to involve the pleura, pain is usually an outstanding feature of the condition. Soon the patient will run a septic temperature, and will have night sweats and increasing dyspnea. Over the affected side, the respiratory excursion is decreased and dulness, or even flatness, and diminished breath sounds may be noted. A friction rub or râles may be present, depending on the type and extent of the lesion. A roentgenogram may show a thickened pleura or the accumulation of fluid. In the latter instance, a presumptive diagnosis of empyema usually is made. To confirm the diagnosis and determine the character of the lesion, thoracentesis frequently is done. Often the needle is inserted in many places before any fluid is found. If fluid is found, instead of a large quantity, as in ordinary empyema, only from 2 to 5 cc. can be withdrawn into the syringe. This is rather typical of

actinomycosis and is due to the fact that the needle is inserted into one of the small pockets of pus. Sulphur granules often may be found in this fluid.

Once the disease has attacked the pleura it is only a matter of time before the process extends to involve the thoracic cage. The disease extends by direct growth and is especially prone to follow a puncture wound, such as is made in thoracentesis. A thick, leathery, indurated process is present about the involved tissue, which eventually becomes red and tender, and fluctuates. At this time, the patient experiences pain, fever and toxic symptoms. When the abscess is drained the symptoms disappear, but a sinus is formed which drains indefinitely. The natural tendency of the disease is to spread to the surrounding tissue, and this tendency becomes much greater if the sinus heals and prevents free discharge of the fluid. In the course of time, a series of abscesses and as many sinuses form. If there is not ample drainage of these abscesses, the patient feels sick and weak and runs the typical course until drainage is reestablished.

If the disease is contracted by way of the esophagus, the mediastinum and pleura are involved first, and the symptoms will be similar to those described for a similar stage of the disease.

There are a few symptoms which occur with such regularity in the disease that it is worth while to comment on them at length. The data given are based on a study of the symptoms in this series of cases and the cases reviewed from the literature.

In practically all cases of actinomycosis of the thorax, fever develops during the course of the disease. Of the forty cases reviewed, there was a history of fever in thirty-four; in the other six, fever was not mentioned. In this series, nine patients had fever while under observation. The fever is probably due to invasion by a secondary organism; it is usually more pronounced in the evening, although it may occur in the morning. The temperature seldom runs higher than 101 F. If an abscess is present, or if the invasion of secondary organisms is rapid, the temperature may go much higher. Fever due to abscess or empyema is of the septic type, and will disappear soon after adequate drainage is established. Fever due to a bronchopneumonic type of lesion will vary according to the progress of the disease.

Expectoration is present in from 60 to 70 per cent of the cases and varies considerably in amount. It is often streaked with blood, probably on account of suppuration and rupture of peribronchial granulomas. Often it is fetid, reminding one of the sputum in bronchiectasis. Occasionally it is viscous and, on standing, separates into two layers: the upper layer is mucous; the lower layer is viscous and is composed

of a yellow sediment in which the elements of *Actinomyces* may be found.

Hemoptysis is relatively rare. Of forty cases in the literature, in only two had there been definite hemorrhage; in one of these, about 125 cc. of blood had been expectorated. In a third case there had been considerable blood in the sputum for four days. All of these patients died. In the present series there had been sudden hemorrhage from the lung in one case, but subsequent recovery was remarkable. The reason hemorrhage is so rare in actinomycosis of the lung, as Naussac pointed out, is the almost total lack of erosion of the wall of the vessel even "in an abscess undergoing purulent melting." This integrity of the blood vessels is characteristic of actinomycosis and distinguishes it from tuberculosis. As noted, the sputum often is streaked with blood, possibly owing to rupture of peribronchial granulomas.

During the course of the disease, practically every patient suffers pain. The character of the pain may vary greatly. It may be an intermittent "sticking" type felt through the thorax, which is hardly severe enough for the patient to note. In some cases, it may be a sense of constriction through the thorax. When the pleura is involved, the pain is much more severe and may become incapacitating. The character of the pain frequently changes after a few days from a sharp respiratory type to dull, constant pain. Occasionally, the disease spreads to involve the vertebral column and the anterior nerve roots, and causes root pain. Complications, such as rupture of an abscess from the pleural cavity into the peritoneal cavity, producing severe, cramplike pains and collapse, must be kept in mind. The psoas muscle is involved in some cases; frequently, this gives rise to painful contracture which necessitates the application of Buck's extension for relief.

Cough is a symptom in 90 per cent of the cases, although it may not be bothersome. If the disease starts as apparent bronchitis or bronchopneumonia, cough occurs early and may subside as the disease progresses. In other cases, it does not appear until late. Usually, the cough is productive; less frequently, it is a nonproductive, hacking cough, and occasionally it is paroxysmal.

The sense of weakness may be the first and chief complaint. Late in the course of the disease, it is a constant complaint. Dyspnea is experienced in about 40 per cent of the cases; it is present when the lung is sufficiently involved to embarrass respiration, and is more commonly present in the sclerotic type of lesion of the lung. Although this symptom may occur early in the course of the disease, it is usually late. The early manifestation of involvement of the pleura is serous

pleuritis, which becomes purulent pleuritis or empyema as a result of the invasion of secondary organisms. An actinomycotic abscess may perforate into the pleura and produce empyema. The empyema pocket may be large, but more often it is small, because of interlacing fibrous adhesions. Anemia is noticeable rather late in the disease in from 65 to 70 per cent of the cases. In this series, the average percentage of hemoglobin was 67, but in some cases the percentage of hemoglobin was as low as 29, and transfusion had to be given. Marked loss of weight is the rule. In this series, the average loss of weight was 34 pounds (15.4 Kg.). In an occasional case, weight will be gained for a time at least. Night sweats are noted only if the condition is definitely septic or the patient is markedly debilitated. Clubbed fingers were evident in only one case, and in this case empyema had developed. In all probability, such a condition occurs only in the presence of associated purulent pulmonary complications. Because of the close proximity of the diseased pleura to the thoracic wall, the latter becomes involved in from 80 to 90 per cent of the cases. A fistulous opening from the pleural cavity to the soft tissue of the thorax frequently is found.

In the region of the abscesses there may be definite erosion of the ribs. The ribs were definitely involved in 25 per cent of the cases noted in the literature, whereas the vertebrae were involved in 10 per cent. Occasionally, actinomycotic osteomyelitis may be present. In one of the cases there was osteomyelitis of the sternum.

Diagnosis.—The diagnosis depends on the finding of *Actinomyces* in the sputum or in the pus of an abscess or sinus or on demonstration of the actinomycotic lesion in a histologic specimen. One may be aided in making a presumptive diagnosis of actinomycosis by: (1) the character of the sputum; (2) persistent symptoms of bronchopneumonia; (3) induration and formation of abscesses and sinuses in the soft tissue of the thorax, and (4) examination by roentgen ray.

Differential Diagnosis.—The long duration of symptoms practically rules out simple pneumonia. Tuberculosis is perhaps the most likely presumptive diagnosis. Against this diagnosis are the following facts: The lesion is basal; repeated examinations of the sputum are negative for bacilli of tuberculosis, and the roentgenologic data are not typical of tuberculosis. The correct diagnosis is made solely on the presence of *Actinomyces* in the sputum. At this stage, this organism is found with relative infrequency.

Treatment.—The patient should be put on a full diet and be given plenty of sunshine and fresh air. Special forms of treatment also have been found to be helpful.

The use of potassium iodide in the treatment for actinomycosis is empiric. Its action, as stated by Lieblein,[6] is to bring about solution of the cellular infiltrative process about the abscess and the consequent discharge of *Actinomyces*, in imitation of nature's own method of healing. Several cases have been reported in which the organisms were found in great numbers in the sputum prior to the use of the drug but disappeared rapidly under its use. A short time later, at necropsy, *Actinomyces* could be demonstrated only by the most diligent search, although the pathologic structural changes were present in abundance. Progressively increasing doses of saturated solution of potassium iodide are given three times a day until the patient is taking 600 minims (36.96 cc.) daily, or until the point of tolerance is reached. Chitty[7] prefers the use of tincture of iodine to potassium iodide. He gives from 6 to 10 minims (0.37 to 0.61 cc.) of the tincture of iodine in milk, three or four times daily, and his results are rather striking. The iodine apparently is readily absorbed when given in this manner. The intravenous use of sodium iodide has no advantage over the oral administration of potassium iodide.

Treatment by roentgen ray and radium has given excellent results in certain cases. The symptoms have been attentuated, and life apparently has been prolonged in many cases; in some cases on record the disease apparently has been arrested by the use of roentgen ray and radium. The success of such treatment depends necessarily on the stage to which the disease has progressed and on the site of the lesion. Surgical procedures are indicated only to establish and maintain ample drainage of abscesses and of empyema pockets.

Course.—In the majority of the cases the course is progressively downward; it is characterized by increasing weakness, dyspnea, cough, pain, loss of weight and increasing anemia. The outcome is usually fatal, and death results from the debilitating effects of the disease or from secondary infection. There are a few chronic cases, however, in which the symptoms extend over a period of years. In such cases the patients usually feel well if there is ample drainage of the abscesses or empyema pockets. If an abscess forms, or if there is insufficient drainage, the patient experiences toxic symptoms of a varying degree of severity. If there is ample drainage of the abscess, the patient regains a fair state of health. In other cases, the disease apparently has been arrested. The average duration of symptoms, from probable onset to death, in the twenty-seven cases recorded in the literature, was

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6. Lieblein, quoted by Erving, W. G.: Actinomycosis Hominis in America, with Report of Six Cases, Bull. Johns Hopkins Hosp. **13**:261, 1902.

7. Chitty, Hubert: Actinomycosis Successfully Treated by Iodine in Milk, Brit. M. J. **1**:418, 1926.

eight months. The vast difference in duration of symptoms between the series reviewed in the literature and the series seen at the clinic, probably is due to one or both of two factors. The more important factor of the two, perhaps, is the advanced stage of the disease when the patients whose cases are recorded in the literature presented themselves for treatment. The second factor is concerned with the treatment for the disease. Many of the cases recorded in the literature occurred before the day of treatment by roentgen ray. The average duration of symptoms from the probable date of onset of the disease to death,

TABLE 3.—*Summary of Symptoms in Thirteen Cases of Primary Actinomycosis of the Thorax Seen at the Mayo Clinic*

Symptoms	Present	Not Recorded	Absent	Average
Fever	9	..	4	..
Cough	9	3	1	..
Night sweats	5	6	2	..
Pleurisy	10	1	2	..
Weakness	11	2	..	..
Pain	11	2	..	..
Expectoration	6	6	1	..
Loss of weight, pounds	..	..	..	34
Hemoglobin, per cent	..	..	..	67
Sinuses	10	1	2	..
Empyema	3	9	1	..
Blood pressure: Systolic	..	..	..	123
Diastolic	..	..	..	77

TABLE 4.—*Result of Treatment and Duration of Symptoms in Forty Cases of Primary Actinomycosis of the Thorax Recorded in the Literature*

Result	Cases	Per Cent	Duration of Symptoms, Months	Duration of Symptoms Not Given, Cases
Dead	27	67.5	8	5
No improvement	6	15.0	14	1
Improved	4	10.0	24	..
Arrested	1	2.5	2	..
Not given	2	5.0	..	..

in the series observed at the clinic, was twenty-nine months. The average duration of symptoms between registration at the clinic and establishment of the diagnosis was fifteen months.

Results of Treatment.—Of the thirteen cases in the present series, death has occurred in six (47 per cent). In two cases there has not been improvement; in one case there has been apparent improvement, and in another case the condition seems to have been completely arrested. In three cases, follow-up data have not been obtained (table 3).

If the results obtained in this series are compared with the results obtained in the cases recorded in the literature (table 4), one finds in

the latter that in the forty cases, twenty-seven patients (67 per cent) died. In six cases improvement did not occur; temporary improvement was noted in five, and there were no follow-up data in two cases. One patient was reported as well, but the duration of the "arrested stage" in this case was only two months, a period far too short to pronounce a patient "well" in this disease.

I believe that a combination treatment, consisting of the administration to tolerance of a saturated solution of potassium iodide, together with treatment by roentgen ray and radium and ample drainage, when indicated, has definitely prolonged the life of the patient and attenuated the symptoms, particularly in cases in which treatment was administered early in the course of the disease.

Prognosis.—The disease is almost always eventually fatal. In a report of eighty-seven cases of actinomycosis seen in Norway, Harbitz and Grondahl [8] stated that the thorax was involved in 23 per cent. All of these patients died. Other authors have stated that the mortality rate is from 60 to 75 per cent. Such an estimate is based on the known death rate in a series and does not take into consideration the probable mortality in those cases listed as unimproved, improved and so forth. The duration of symptoms from onset to death is from eighteen months to two years. In an occasional case, to the contrary, the course will be markedly rapid, and death will occur in from one to five months. The symptoms in a few cases will be drawn out over a period of from six to eight years. In rare instances, there seems to be spontaneous and final arrest of the process.

SECONDARY LESIONS

This study is based on data concerning sixteen patients suffering from actinomycosis with secondary involvement of the thorax. In this series, the primary lesion was in the abdomen in 94 per cent of the cases. In one case the primary lesion was on the tibia; many years later, an esophagobronchial fistula developed with secondary pulmonary involvement. The thorax becomes involved secondarily by direct extension, by dissemination through the blood stream or by the introduction of the organism into the mouth.

The right side of the thorax was affected in ten cases (63 per cent, table 6). Involvement was of the left side in two cases; of the right or left side in one case, and of both right and left sides in three cases. The predominance of the condition in the right side is readily explained by the fact that the majority of the primary lesions are in the right

8. Harbitz, Frances; and Grondahl, N. B.: Actinomycosis in Norway: Studies in the Etiology, Modes of Infection and Treatment, Am. J. M. Sc. **142**: 386, 1911.

side of the abdomen, and that the thorax becomes involved secondarily by direct extension in a high percentage of cases. If the disease is carried to the lungs by the blood stream, either or both lungs may be affected.

The lesions encountered in secondary actinomycosis of the thorax are similar to those in primary actinomycosis of the thorax. The symptoms and the course of the disease are similar (tables 5 and 6). With secondary thoracic involvement, the patient complains of greater weakness, and night sweats are more troublesome. Anemia is more

TABLE 5.—*The Primary Site of Actinomycosis in Sixteen Cases Involving the Thorax, Secondarily*

Primary Site of Lesion	Cases	Per Cent
Ileocecal region or appendix	10	62.5
Appendix or sigmoid	1	6.3
Tonsil or appendix	1	6.3
Gallbladder or appendix	1	6.3
Abdominal wall	1	6.3
Tibia or larynx	1	6.3
Right upper part of abdomen	1	6.3

TABLE 6.—*Summary of Symptoms in Sixteen Cases of Actinomycosis with Secondary Involvement of the Thorax*

Symptoms	Present	Not Recorded	Absent	Average
Fever	9	4	3	....
Cough	6	6	4	....
Night sweats	11	3	2	....
Pleurisy	11	3	2	....
Weakness	10	5	1	....
Pain	14	2	..	....
Expectoration	7	8	1	....
Sinus	13	..	3	....
Empyema	3	4	9	....
Hemoglobin, per cent	..	..	..	51.5
Loss of weight, pounds	..	..	..	34.5

pronounced in the secondary type, whereas the loss in weight is about the same in both types.

When the thorax becomes involved secondarily, the disease usually has progressed beyond the point where one could hope to arrest it. The symptoms may be attentuated and life prolonged by following the line of treatment outlined for primary actinomycosis of the thorax. In sixteen cases, nine patients (56 per cent) died. Three patients were improved. Follow-up data were not obtainable in four cases.

The average duration of symptoms from the date of probable onset of the disease to death was three years. The duration of symptoms in one case was extremely long. If this case were not included in computing the duration of symptoms, the average duration of symptoms would be eighteen months (figs. 1 to 4).

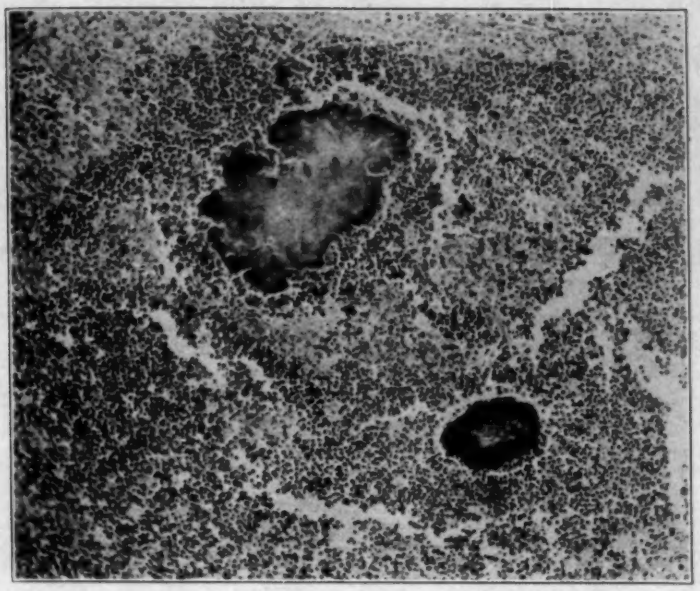

Fig. 1.—Actinomycotic abscess of the lung in which two granules can be seen is shown; hematoxylin and eosin; × 100.

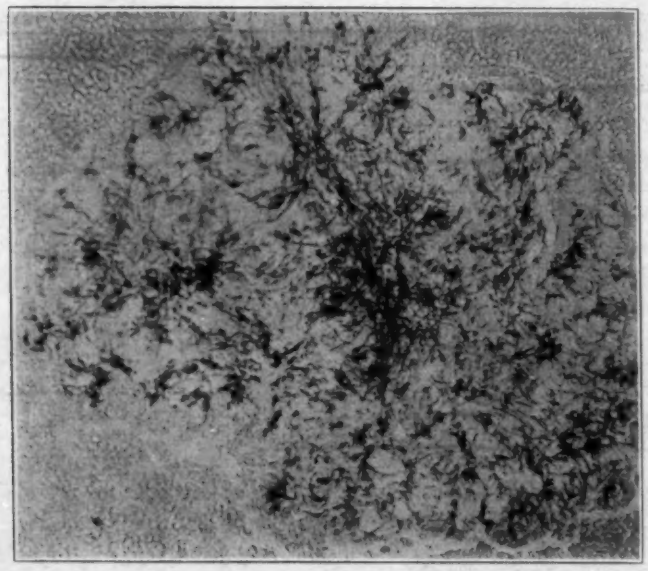

Fig. 2.—An actinomycotic lesion in which the mycelia are well shown; × 150.

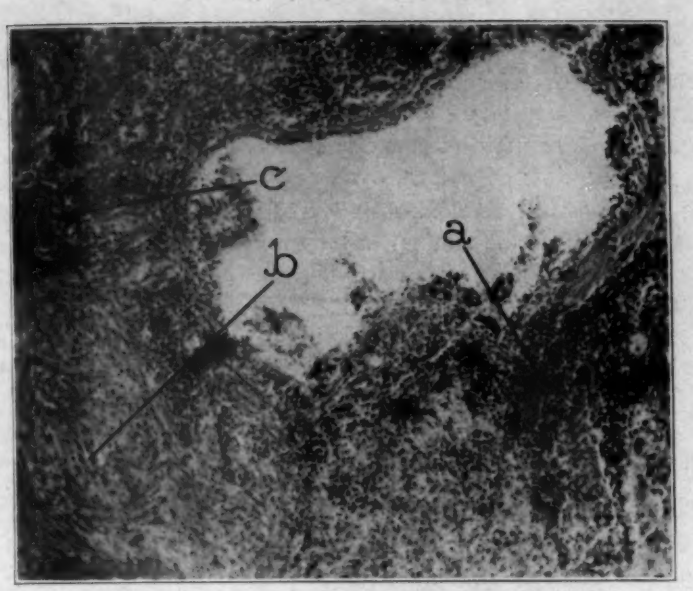

Fig. 3.—A large blood vessel is surrounded by granulation tissue of an actinomycotic lesion of the lung; *a*, an abscess just lateral to the vessel is seen to involve its wall; *b*, whorls in granulation tissue, and *c*, lung is laden with carbon pigment; hematoxylin and eosin; × 75.

Fig. 4.—A bronchus is filled with detritus of an actinomycotic lesion; *a*, actinomyces; hematoxylin and eosin; × 75.

SUMMARY

The symptoms of actinomycosis of the thorax may simulate those of bronchitis, bronchopneumonia, pulmonary abscess and pulmonary tuberculosis. The more common symptoms are: fever, cough, sputum, pain, weakness, loss of weight, dyspnea, anemia and external abscesses.

The diagnosis of actinomycosis is made: (1) by demonstrating the sulphur granule in the sputum, in empyema fluid or in the pus from an abscess, or (2) by demonstrating the actinomycotic lesion in a histologic specimen.

Treatment should be directed at improving the general health, the administration to tolerance of potassium iodide, the drainage of abscesses and empyema pockets, and the proper use of roentgen ray and radium.

The disease is fatal in from 60 to 70 per cent of the cases.

INTRACRANIAL CALCIFICATION

WITH PARTICULAR REFERENCE TO THAT OCCURRING IN THE GLIOMAS *

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LOS ANGELES

Areas of intracranial calcification are not uncommonly seen in roentgenograms of the skull, associated with conditions of both a physiologic and a pathologic nature. This is particularly true since the Bucky diaphragm has made it possible to demonstrate the minute details of the skull and any calcareous material of any magnitude within it. The question will consequently arise as to the nature of the associated lesion, particularly if the roentgenograms were taken with the hope of establishing the diagnosis of an obscure disease of the brain. It is our purpose in this study to note first the pathologic possibilities and then to discuss more in detail calcification within intracranial tumors, particularly the gliomas. This is of special importance to the surgeon, for a calcified tumor not only gives positive testimony as to its situation, but also encourages him to believe that it has benign tendencies.

CALCIFICATION IN REGRESSIVE AND DEGENERATIVE PROCESSES

Calcification in the pineal body may be seen in the majority of roentgenograms of the skull of adults. Several years ago, Schüller [1] called attention to the dislocation of calcified pineal bodies from the midline in intracranial tumors, a fact reaffirmed more recently by Naffziger.[2] Vastine and Kinney,[3] in reviewing the roentgenograms in 616 cases of suspected intracranial tumor in which calcification of the pineal bodies was observed, made a note of its position in relation to the anteroposterior and vertical diameters of the skull as measured on the lateral plate. They found that its dislocation beyond certain limits is a valuable aid in the localization of intracranial lesions. Calcification is

* Submitted for publication, March 14, 1930.

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1. Schüller, Arthur: Roentgen Diagnosis of Diseases of the Head, translation by Stocking, St. Louis, C. V. Mosby Company, 1918, p. 156.

2. Naffziger, H. C.: A Method for the Localization of Brain Tumors: The Pineal Shift, Surg. Gynec. Obst. **40**:481 (April) 1925.

3. Vastine, J. H., and Kinney, K. K.: The Pineal Shadow as an Aid in the Localization of Brain Tumors, Am. J. Roentgenol. **17**:320 (March) 1927.

also occasionally seen in the choroid plexuses of the lateral ventricles, appearing as flocculent masses on one or both sides as oriented in stereoroentgenograms. While its significance is not clear, calcification in these structures may be of an irritative or chronic inflammatory nature.

At times, calcification in sclerosed vessels forming the circle of Willis may be observed in the roentgenogram.[4] Chronic inflammatory conditions are probably responsible for the presence of the calcification and ossification in the arachnoid and dura mater.[5] True bone formation of any size is found most frequently in the dura, especially in its reduplication, the falx cerebri.[6] Calcium is occasionally deposited in traumatic scars of the brain, softenings of the brain and old cerebral hemorrhages. It may also be found in the form of small granules in chronic degenerative and inflammatory processes, such as Parkinson's disease,[7] encephalitis,[8] malaria,[9] and in toxic conditions, such as carbon monoxide poisoning.[10] Macewen[11] found calcium in the walls of chronic abscesses of the brain.

It may also occur in that borderline heterotropia, lying between the congenital malformations on one hand and true tumors on the other—tuberous sclerosis. In this condition, calcium is commonly found in the walls of the small blood vessels[12] and may be responsible for the convulsions characteristic of the lesion. The surgical removal of tissue

4. Holmes, G. W., and Ruggles, H. E.: Roentgen Interpretation, ed. 3, Philadelphia, Lea & Febiger, 1926, p. 117.

5. Cushing, Harvey; and Weed, L. H.: Studies on the Cerebro-Spinal Fluid and Its Pathway: IX. Calcareous and Osseous Deposits in the Arachnoidea, Bull. Johns Hopkins Hosp. **26**:367 (Nov.) 1915. Halstead, A. E., and Christopher, F.: Calcification and Ossifications of the Meninges, Arch. Surg. **6**:847 (May) 1923.

6. Dr. Ray A. Carter, roentgenologist to this hospital, called our attention to the occurrence of calcification in the attachments of the tentorium to the clinoids. In the roentgenogram, small masses of calcareous material appeared as hornlike projections of the posterior clinoids.

7. McAlpine, Douglas: The Pathology of the Parkinsonian Syndrome Following Encephalitis Lethargica, with a Note on the Occurrence of Calcification in This Disease, Brain **46**:255, 1923.

8. Calcification in encephalitis has been observed by others (Spatz: Ztschr. f. d. ges. Neurol. u. Psychiat. **77**:261, 1922), but the essential process is probably the same in this as in other chronic degenerative or toxic conditions. The calcareous material seems to be deposited chiefly in the walls of the blood vessels.

9. Seifarth: Deutsches Arch. f. klin. Med., 1921, vol. 134, quoted by Kaufmann [footnote 12, p. 1919].

10. Eaves, E. C.: A Contribution to the Study of Deposits Containing Calcium and Iron in the Brain, Brain **49**:307, 1926.

11. Macewen, William: Pyogenic Infective Diseases of the Brain and Spinal Cord, New York, The Macmillan Company, 1893, p. 109.

12. Kaufmann, Edward: Pathology for Students and Practitioners, translation by Reimann, Philadelphia, P. Blakiston's Son & Company, 1929, vol. 3, p. 1909.

in which calcification was found in blood vessels was recently reported by Geyelin and Penfield;[13] the lesion was probably of this type.

CALCIFICATION IN INTRACRANIAL TUMORS

Calcareous deposits have been known to occur in almost every variety of primary new-growth that compromises the intracranial space. It has been observed in gummas and tuberculomas of the brain, although we have not encountered it in any such lesions coming under our direct observation. It is also rarely found in the walls of parasitic cysts, where it assumes a more or less crescentic shape conforming to the walls of the cyst. Calcification in these conditions is indicative of a quiescent process.

The presence of flocculent shadows in or above the sella in roentgenograms of cysts arising from the remains of the craniopharyngeal canal is of particular interest. Luger,[14] in reviewing the literature, indicated that calcification in this type of tumor has been noted for many years both in the roentgenogram and in the gross specimen. He mentioned the cases of Algyogyis, Sprinzels, Engelman, Erdheim and Walker, and the possible cases of Aschoff, Benda, Bregman and Steinhaus, and Boryces and Radla. Heuer and Dandy[15] found one case of this type of tumor in the roentgenographic studies of a hundred consecutive cases of tumor of the brain. Recently, in a more comprehensive report, McKenzie and Sosman[16] considered in greater detail the type and distribution of the calcareous particles in the walls of the cysts. They found that it occurred in 70 per cent of the cases, its appearance in the roentgenogram constituting thereby a valuable diagnostic sign.

While aneurysms of the larger cerebral vessels have been recognized for almost two hundred years, until recently little or no attention has been paid to calcification occurring in their walls. Schüller[1] seems to have been the first to call attention to the characteristic crescent-shaped plaques in lateral roentgenograms of the skull. Heuer and Dandy[15] reported a typical case in their series. Sosman and Vogt,[17] in reporting

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13. Geyelin, H. R., and Penfield, Wilder: Cerebral Calcification Epilepsy: Endarteritis Calcificans Cerebri, Arch. Neurol. & Psychiat. **21**:1020 (May) 1929.

14. Luger, Alfred: Zur Kenntnis der im Röntgenbild sichtbaren Hirntumoren mit besonder Berüchsichtigung der Hypophysengangsgeschwülste, Fortschr. a. d. Geb. d. Röntgenstrahlen **24**:605, 1914.

15. Heuer, G. J., and Dandy, W. E.: Roentgenography in the Localization of Brain Tumors, Based upon a Series of One Hundred Consecutive Cases, Bull. Johns Hopkins Hosp. **26**:311 (Nov.) 1916. In this contribution, the authors note the early roentgenographic demonstration of calcification in intracranial lesions. Among others are mentioned calcification in a gumma (Lichtheim), cysticercus cyst (Stieda), abscess of the brain (Sträter), pineal tumor (Grunmach) and tumors of the brain (probably gliomas) by Schüller and Klineberger.

16. McKenzie, K. G., and Sosman, M. C.: The Roentgenological Diagnosis of Cranio-Pharyngeal Pouch Tumors, Am. J. Roentgenol. **11**:171 (Feb.) 1924.

17. Sosman, M. C., and Vogt, E. C.: Aneurysms of the Internal Carotid Artery and the Circle of Willis, Am. J. Roentgenol. **15**:122 (Feb.) 1926.

a series of ten cases verified at autopsy, considered two that gave roentgenographic evidence of the plaques. In a second series of ten unverified cases, six showed the typical semilunar plaques in their walls. Such observations are indicative of the larger aneurysms, as the smaller forms give no roentgenographic evidence of their presence, except for a minor degree of erosion of the clinoids.

Tumors that had their origin from the meninges were probably the first to be demonstrated roentgenographically. The historical cases of Obici and Bollici,[18] and of Mills and Pfahler [19] were undoubtedly of the type known as "endotheliomas" and more recently as meningiomas or meningeal fibroblastomas. There are several roentgenographic characteristics of this form of intracranial tumor, as has been emphasized by Sosman and Putnam,[20] but the one which concerns us in this connection is that of calcification within the tumor itself. This is rather rare as far as the larger masses visible roentgenographically are concerned, but not infrequently small granules of calcareous material are encountered in the gross specimen. These are probably too small to be seen in the roentgenogram, their shadow being "burned out" in the exposure necessary to get clear detail in the skull.

Mention has been made in the literature of shadows in the sella observed in roentgenograms of the skull in cases in which a pituitary tumor was demonstrated at necropsy.[21] That true calcifications may occur in the pituitary adenomas has been known for some time, but verification for some reason has been delayed until recently. Deery,[22] in a series of 285 pituitary adenomas studied at Cushing's clinic, found 19 in which shadows of calcium could be seen in the roentgenogram. The calcareous material of one of these tumors was subsequently demonstrated histologically.

Calcium has been found in some of the cases of angiomas of the cerebral vessels. In their monograph, Cushing and Bailey [23] collected

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18. Obici and Bollici: Applicazione dei raggi "x" alla diagnosi di sede dei corpi estranei della testa e dei tumori intracranici, Riv. di patol. nerv. **11**:433, 1897, quoted by Sosman and Putnam (footnote 20).

19. Mills, C. K., and Pfahler, G. E.: Tumor of the Brain Localized Clinically and by the Roentgen Rays, Philadelphia M. J. **9**:268 (Feb. 8) 1902. Mills, C. K.; Pfahler, G. E., and Deaver, J. B.: An Additional Case of Tumor of the Brain Localized Clinically and by the Roentgen Rays, Philadelphia M. J. **10**:439 (Sept. 27) 1902.

20. Sosman, M. C., and Putnam, T. J.: Roentgenological Aspects of Brain Tumors: Meningiomas, Am. J. Roentgenol. **13**:1 (Jan.) 1925.

21. Marques and Peyron: Arch. d'élect. méd., 1913, p. 349, quoted by Luger (footnote 14). Rotky: Fortschr. a. d. Geb. d. Röntgenstrahlen, vol. 14, quoted by Luger (footnote 14).

22. Deery, E. M.: Note on Calcification in Pituitary Adenomas, Endocrinology **13**:455 (Sept.-Oct.) 1929.

23. Cushing, H., and Bailey, P.: Tumors Arising from the Blood-vessels of the Brain, Springfield and Baltimore, Charles C. Thomas, 1928, p. 25.

the reports of several cases, in most of which the tumor was found in the occipital lobe. The calcareous material is found in the walls of the anomalous vessels, the tortuous course of which is rather characteristic. Calcification is not uncommon in pinealomas and teratomas of the pineal body.[24]

CALCIFICATION IN TUMORS OF THE GLIOMA GROUP

In spite of their comparatively more rapid growth, the gliomas in many instances tend to undergo calcareous change. In this respect they are eclipsed only by congenital pituitary cysts and perhaps by aneurysms and anomalies of the blood vessels (angiomas). It is evident from our studies that the process occurs far more commonly than is usually suspected, although roentgenographic evidence of it is not always found, because calcareous material occurs in such minute particles. Van Dessel,[25] in a study of 1,111 cases of tumor of the brain at Cushing's clinic, found 40 that gave roentgenographic or pathologic evidence of calcareous material in their substance. Of these growths, 16 were histologically verified, 9 of which were astrocytomas, 4 oligodendrogliomas, 2 neuroblastomas and 1 an ependymal glioma. Sosman[26] concluded that from 10 to 12 per cent of gliomas are demonstrable in the roentgenograph. Bailey and Cushing[27] referred in a special way to calcareous material in oligodendrogliomas and neuroblastomas.

Historically speaking, Strom,[28] in his treatise on intracranial calcification in general, cited the cases of Fittig and Oppenheim as the only cases of gliomas containing calcium which had been demonstrated roentgenographically. In the same year, Souques[29] despaired of the value of the

24. Horrax, G., and Bailey, P.: Tumors of the Pineal Body, Arch. Neurol. & Psychiat. **13**:432 (April) 1925. True osteomas of the brain do occur but they are exceedingly rare. They are usually small in size and are often located in the floor of the third ventricle. They should not be confused with "brain stones," masses of calcareous material probably deposited at the site of old hemorrhages or softenings. Buckley recently reviewed the literature and reported a case of this kind (Buckley, R. C.: Intracerebral Tumors, Arch. Neurol. & Psychiat. **23**:1203 [June] 1930).

25. Van Dessel, Arthur: L'incidence et la processus de calcification dans les gliomes, Arch. franco-belges de chir. **28**:845 (Oct.) 1925.

26. Sosman, M. C.: Radiology as an Aid in the Diagnosis of Skull and Intracranial Lesions, Radiology **9**:396 (Nov.) 1927.

27. Bailey, P., and Cushing, H.: Tumors of the Glioma Group, Philadelphia, J. B. Lippincott Company, 1926, p. 132. In a recent contribution, Bailey and Bucy (J. Path. & Bact. **32**:735 [Oct.] 1929) stated that oligodendrogliomas are almost invariably calcified.

28. Strom, S.: Ueber die Röntgendiagnostik intrakranieler Verkalkungen, Fortschr. a. d. Geb. d. Röntgenstrahlen **27**:577, 1921.

29. Souques, A.: Diagnostic du siège et de la nature d'une variété de tumeurs cérébrales (psammomes ou sarcomes angiolithiques) par la radiographie, Rev. neurol. **37**:984, 1921.

roentgen ray in the diagnosis of intracranial tumors, although he was able to visualize a "psammoma" by this means. Heuer and Dandy,[15] in 6 cases demonstrated roentgenographically in a series of 100, found a growth that was probably a glioma. Newell [30] reported 3 verified cases of glioma containing calcareous material.

From a histologic standpoint, calcification has been found in gliomas by numerous investigators. It was observed by Perkins [31] and Bielschowsky and Henneberg [32] in cases of more rare types of gliomas, the gangliogliomas. Rosenblath [33] and Fraenkel [34] found calcareous material in the wall of gliomatous cysts. Olivecrona [35] found it but once in a series of 37 gliomas verified at operation and necropsy; and in this instance it occurred in the wall of a gliomatous cyst. Globus and Strauss [36] found calcium in one of their cases of spongioblastoma multiforme. In a series of 30 cases of the same glioma, Carmichael [37] encountered 3 in which calcareous degeneration had occurred in the more central portions. Medakovitch [38] found calcification in 3 gliomas in a series of 24 cases. Other scattered cases have been mentioned, but complete descriptions are lacking or the literature is not available to us at this time.[39]

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30. Newell, R. R.: Calcification in Brain Tumors, S. Clin. North America **3**:775 (June) 1923.

31. Perkins, O. C.: Ganglioglioma, Arch. Path. **2**:11 (July) 1926. Calcareous nodules were found by MacPherson in a similar tumor arising in the floor of the third ventricle (Arb. a. d. neurol. Inst. **27**:123, 1925).

32. Bielschowsky, Max; and Henneberg, R.: Über Bau und Histogenese der zentralen Ganglioglioneurome, Monatschr. f. Psychiat. u. Neurol. **68**:21 (March) 1928.

33. Rosenblath, W.: Ein Beitrag zur Lehre von den Geschwülsten des Zentralnervensystems, Deutsche Ztschr. f. Nervenh. **31**:335, 1906.

34. Fraenkel, Konrad: Zur Pathogenese der Gehirncysten, Virchows Arch. f. path. Anat. **230**:479, 1921.

35. Olivecrona, Herbert: Die chirurgische Behandlung der Gehirntumoren, Berlin, Julius Springer, 1927, p. 59.

36. Globus, J. H., and Strauss, I.: Spongioblastoma Multiforme, a Primary Form of Brain Neoplasm: Its Clinical and Anatomic Features, Arch. Neurol. & Psychiat. **14**:188 (Aug.) 1925.

37. Carmichael, E. A.: Cerebral Gliomata, J. Path. & Bact. **31**:493, 1928.

38. Medakovitch, Georges: Contribution a l'étude anatomique du gliome, Thèse de Paris, 1922.

39. Calcification in what may be papillomas of the choroid plexus have been described by Oppenheim and Rheindorf. That of Arnold seems to be an "endothelioma" of the choroid plexus of the third ventricle (Schüller [footnote 1, reference on p. 157]). In fifty-five cases of cerebral neoplasms from Mott's laboratory, Weed found calcification in twenty-two (40 per cent) (Weed, L. H.: A Note on Calcification in Cerebral Neoplasms, Arch. Neurol. & Psychiat. **6**:190, 1914). He classified the morphology of the calcified bodies as punctate, vascular, trabecular, amorphous and periarterial. Calcium was found in a third of the gliomas and in adenomas of the pituitary gland.

OUR SERIES OF VERIFIED CASES

To the present time there are 28 cases of verified gliomas in the records of the neurosurgical service of the hospital. A large number of others have been verified at operation or at necropsy but, as the tissue is not available for study, they have not been included in this series. With 2 other cases from extramural sources, we are able to report 10 histologically verified and 2 unverified cases of glioma in which calcification was demonstrable in the roentgenogram or the histologic section or both. As tissue or sections were available in the verified cases, we investigated in detail the histologic aspects of the problem.

CASE 1.—*Ossification in a neurogliablastoma multiforme*[40] *(spongioblastoma multiforme) in the body of the corpus callosum.*

The patient, a Mexican girl, aged 18, was admitted to the hospital in coma on April 26, 1926. Seven years prior to the onset of the present illness, the patient had spells of vomiting associated with severe headaches for a period of three months. During this time there was a gradual failure of vision, which resulted in complete blindness. At the end of the period all symptoms cleared up without treatment, the patient remaining well until two weeks before admittance to the hospital. At this time the headaches recurred. Three days before coming into the hospital, she began to have generalized convulsions and vomiting.

On examination the patient appeared to be in deep coma marked by frequent convulsive seizures of the right side of the body and conjugate deviation of the head and eyes to the right. She was rather obese, the distribution of the adiposity resembling that seen in pituitary disturbance. The pupils were widely dilated, and bilateral secondary optic atrophy was found. A lumbar puncture showed the spinal fluid to be under increased pressure. Laboratory analysis revealed a two plus Wassermann reaction and a paretic type of colloidal gold curve.

Stereoscopic films revealed a small round mass of calcification lying just above and slightly posterior to the sella turcica in the midline of the skull (fig. 1).

The patient remained about the same during the period of observation in the hospital. She died rather suddenly before surgical exploration was attempted.

At necropsy, a fairly circumscribed tumor was found in the midline of the brain and extending down into the third ventricle, apparently having its origin from the inferior part of the body of the corpus callosum. A compact mass of bone was found in the tumor. Histologic studies revealed firm, scarlike tissue about the bony mass, while in the peripheral portions a loosely arranged tumor stroma was found containing cells typical of neurogliablastoma multiforme.

Comment.—It seems apparent that seven years prior to the illness which brought about the death of the patient, a rapidly growing tumor developed from the tissues of the corpus callosum, which, after a

40. We have come to indicate the tumor, commonly known as "gliosarcoma" or more recently as "spongioblastoma multiforme," as a neurogliablastoma. In a histologic study of a series of cases in this laboratory, we found typical and well developed neuroblasts as well as gliablasts. The primary cell must therefore be bipotential as is the case in the essential elements of the medulloblastoma cerebelli. A complete report is to appear soon.

fulminant course of three months, suddenly ceased to grow for some unaccountable reason. The necrosis which took place at that time probably was the starting point for the formation of bone, as was described by Mallory.[41] A renewed growth of the tumor came about, which hastened the death of the patient after a short course of eight weeks. This was the only case in the series in which actual bone was found.

CASE 2.—*Multiple calcerous nodules in an atypical glioma of the left frontal lobe.*

A linotype operator, aged 45, was admitted to the hospital on Sept. 9, 1926, complaining of headaches, vomiting, failing vision and weakness in the right arm and hand, all of six months' duration.

Fig. 1 (case 1).—Mass of calcification above the sella turcica. At necropsy this proved to be bone formation within a neurogliablastoma multiforme of the corpus callosum.

At the time of admittance the patient was found to be rather somnolent and presented a bilateral choked disk, more marked on the left side, associated with weakness of the right side of the face and spastic paralysis of the right arm. The deep reflexes were increased on the right side, and Babinski's sign was present on this side. There was also a slight tremor in the left extremities and left ankle clonus.

Stereoscopic films of the skull showed numerous small calcareous particles scattered throughout the left frontal region. There was an associated thinning of the frontal bone on the left side (fig. 2).

41. Mallory, F.: Principles of Pathologic Histology, Philadelphia, W. B. Saunders Company, 1914, pp. 355, 444 and 627.

A left frontal exploration was undertaken on September 30, and a soft, infiltrating glioma was exposed which seemed to fill the entire left frontal lobe. The patient's condition was critical, so complete removal was not undertaken. He died a few hours later.

As necropsy was refused, the exact extent and relationships of the tumor were not determined. The tissue removed at the time of operation was reddish gray and soft and it contained numerous small calcareous particles. Histologic studies showed the tumor to be rather cellular, the nuclei of the constituent cells being more uniform in size than is usually encountered in malignant invasive gliomas of the cerebral hemispheres. In architecture and cellular detail it resembled more nearly medulloblastoma. No further tissue being available at the time of this study, a determination of its exact nature could not be made.

Comment.—The distribution of the calcareous particles in this case was interesting, as they were found throughout the entire left frontal

Fig. 2 (case 2).—Diffuse calcification in a glioma of the left frontal lobe.

region. In no other case in our series was such a uniform involvement of the tumor tissue found.

CASE 3.—*Calcification in a fibrillary astrocytoma of the left parietal lobe.*

A Negro chauffeur, aged 26, was admitted to the hospital on July 20, 1927, with the complaint of left sided fronto-occipital headaches, vertigo and, for the past three months, double vision and failing vision. In the past year he had two generalized convulsions. His condition grew steadily worse in spite of a submucous resection and anesthetization of the sphenopalatine ganglion.

On examination bilateral choked disk was found, associated with a bilaterally diminished visual acuity. Aside from a slight weakness of the right hand there were no other positive neurologic observations. Lumbar puncture revealed the cerebrospinal fluid to be under greatly increased pressure but otherwise normal.

Stereoscopic films of the skull showed a large number of calcified particles in the posterior parietal region on the left side associated with a thinning of the vault over the calcified area (fig. 3).

A left osteoplastic flap was turned down on July 28, 1927, and an underlying tumor could be seen through a thinned dura. When the dura was opened, a large cyst ruptured spontaneously. A firm, well delineated tumor was entirely removed by blunt dissection. After a somewhat stormy postoperative course, the patient made a complete recovery.

At the time of the last examination, over two years after the operation, the patient was free from symptoms and worked every day. Roentgenographic examination of the skull revealed no further evidence of calcification.

The tissue removed at operation was rather firm, friable and reddish, and it contained numerous calcareous particles. Histologic studies showed that it was comparatively acellular and had a stroma characteristic of a fibrillary astrocytoma.

Comment.—The clinical course was rather short for an astrocytoma. The calcareous particles, found particularly in the margin of the tumor,

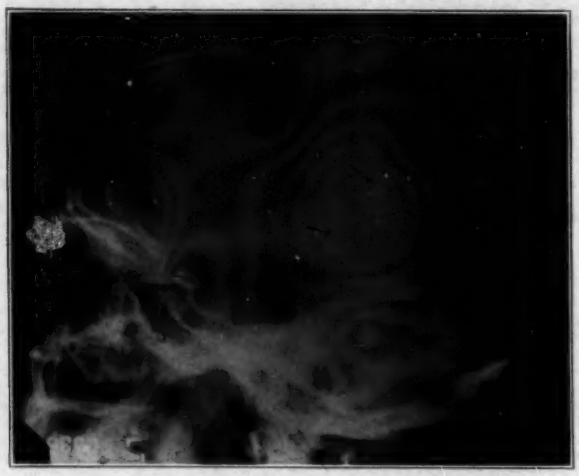

Fig. 3 (case 3).—Flocculent calcification in an astrocytoma fibrillare of the left parietal lobe.

served to delineate it very well on the roentgenogram. Complete extirpation was apparently done in this case and the prognosis was good.

CASE 4.—*Calcification in a neurogliablastoma multiforme of the right frontal lobe.*

A cabinet maker, white, aged 42, was admitted to the psychopathic ward of the hospital for observation. His wife stated that he had been undergoing marked mental changes for the past six months, had complained of headaches for the past five weeks, and more recently had spells of weakness and double vision. After admission to the hospital, he had two jacksonian convulsions involving the left side of the body.

On examination the patient presented marked mental changes, demonstrating typical "Witzelsucht" as described in tumors of the frontal lobe. The disks showed bilateral choking, and there was bilateral anosmia. Some ataxia, past-pointing in the left arm and a Babinski sign on the left were observed.

Stereoscopic films of the skull failed to reveal any evidence of intracranial disease.

After careful study, the patient was transferred to the neurosurgical service. On March 22, 1928, a ventricular puncture was done and air injected. Ventriculograms showed a filling defect of the anterior horn of the right lateral ventricle. A right frontal exploration was attempted on May 10, but had to be abandoned because of the critical condition of the patient. A reexploration a month later revealed an extensive infiltrating glioma of the right frontal lobe, a large portion of which was resected. The patient died five days after operation. Necropsy was refused.

The tissue that was removed at operation was subjected to study and the tumor proved to be a neurogliablastoma multiforme. Small calcareous particles were found in the margin of the tumor.

Comment.—This is another case in which the roentgenograms failed to reveal any evidence of calcification, yet in which the process was clearly shown by microscopic study of the tumor tissue.

CASE 5.—*Calcification in an astrocytoma protoplasmaticum of the left temporoparietal region.*

A white laborer, aged 36, was admitted to the hospital on Oct. 26, 1928, with the complaint of headaches, vomiting, loss of weight and progressive failure of vision of eight months' duration.

At the time of admittance the patient showed marked mental retardation and confusion; he was unable to give a clear account of the history of his illness. He was practically blind, having but a slight degree of light perception in the right visual fields. The pupils were widely dilated and unequal, the right being larger than the left. The optic disks showed a bilateral choking of 5 diopters' elevation. There was a slight right hemiparesis associated with an increase in the deep, and a decrease in the superficial, reflexes on the same side.

Stereoscopic films of the skull revealed flocculent masses of calcareous material in the posterior temporoparietal region of the left side (fig. 4).

On November 15, a left osteoplastic bone flap was turned down and a decompression made. Because of the condition of the patient, further exploration could not be done at the time. Two weeks later the region was reexplored, and a large mass of soft, gelatinous tumor tissue containing calcareous particles was removed. After a somewhat stormy postoperative course, the patient recovered and was discharged on Feb. 15, 1929.

Because of elevation of the bone flap, he was readmitted to the hospital on October 8. At that time a marked weakness of the right arm and leg was noticed. Stereoscopic films of the skull showed the bone flap markedly elevated and riding on the soft tissue swelling at the site of decompression. Calcareous particles were found both within the skull and in the soft tissue mass protruding through the operative defect. On October 17, a reexploration was done, and another large mass of soft gelatinous glioma was resected. When the patient was ready for discharge from the hospital, he showed residual right-sided weakness and almost total blindness.

The tissue recovered at both operative sessions proved to be comparatively acellular and had a stroma of faintly fibrillary character, characteristically of a protoplasmic astrocytoma. Numerous calcareous masses were found throughout the tissue.

Comment.—This rather benign tumor was superficial in its situation, so that it was exposed when the dura was opened. Its extent was well marked in the roentgenogram by the contained calcareous particles, which proved of value to the surgeon when he attempted extirpation. Such cases should have an increasingly good prognosis with the aid of electrosurgical methods.

CASE 6.—*Calcification in a neurogliablastoma multiforme arising in the genu of the corpus callosum.*

A stenographer, white, aged 30, divorced, was admitted to the neurologic service of the hospital on Oct. 4, 1928, with the complaint of ringing in the right ear for six months, generalized convulsions and an ataxic gait for four months. More recently, she had complained of severe headaches and had become incontinent. She had become steadily worse since the onset of her illness, and at the time of admittance she showed drowsiness deepening into stupor.

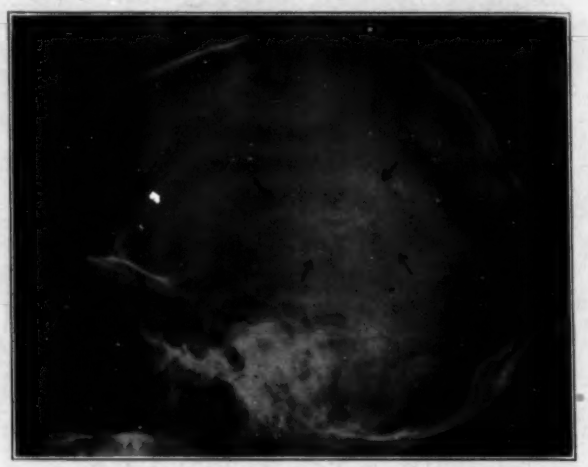

Fig. 4 (case 5).—Calcification in an astrocytoma protoplasmaticum of the left temporoparietal region.

On examination, the patient appeared stuporous, but could be aroused to some extent. Marked mental changes had occurred. The patient was stubborn and refused to answer questions. The pupils were irregular and unequal, the right being larger than the left. The disks were bilaterally edematous, with an elevation of 4 diopters. The extra-ocular muscles on the left side were weak, so that there was little control of movement of the left eyeball.

Stereoscopic films of the skull showed no evidence of intracranial disease.

A lumbar puncture revealed a clear fluid under increased pressure. A ventricular puncture was attempted, but, because of the condition of the patient, had to be abandoned before air was injected. The patient died six days after admittance.

Necropsy revealed a large grayish invasive glioma arising from the genu of the corpus callosum and extending into both frontal lobes. Histologic studies of its tissue showed it to be a typical neurogliablastoma multiforme. Small particles of calcareous material were found in the tumor tissue, particularly near its margins.

Comment.—This case further illustrates the fact that calcification may occur within gliomas without its being demonstrated in the roentgenogram. This may not necessarily be because the films are not clear or are improperly taken, but rather because the calcareous particles may be so small as not to be visualized. In any case when an intracranial tumor is suspected, it is important to have stereoscopic pictures in which details can clearly be made out, so as not to overlook any evidence of value in the diagnosis.

CASE 7.—*Calcification in a neurogliablastoma multiforme of the left parietal lobe.*

A pipefitter, white, aged 49, was admitted to the hospital on Nov. 3, 1928, with the complaint of headaches, vomiting and generalized convulsions of a year's

Fig. 5 (case 7).—Calcification in a neurogliablastoma multiforme of the left parietal lobe.

duration, with recent failure of auditory acuity and mental confusion. The symptoms had progressed in severity from the onset, and it was noticed on the day of admission that the vomiting was definitely projectile.

Examination revealed the patient to be mentally disturbed and totally deaf. The pupils were unequal, the right being larger than the left. There was bilateral choked disk of 4 diopters' elevation. The vestibular responses showed bilateral hypersensitivity, associated with a complete loss of hearing. The deep reflexes were generally increased, and a bilateral Babinski sign was present.

Stereoscopic films of the skull showed flocculent calcareous shadows on the left side of the intracranial space beneath the parietal bone. There was no destruction of the bone in this region, and there were no other positive observations (fig. 5).

Ten days after admittance to the hospital, a left osteoplastic flap was turned down. The dura was found to be under marked tension, and because of the condition of the patient, it was not opened. He died on the day following operation.

At necropsy a yellowish-gray, somewhat degenerated, invasive glioma containing calcareous particles was found involving the left parietal lobe. Microscopic study of the tissue showed it to be a neurogliablastoma multiforme.

Comment.—This case is of particular interest in that the neurologic symptoms and signs were extremely misleading. The marked pressure signs, with bilaterally and equally choked disks and bilateral deafness suggested a lesion of the posterior fossa, possibly a tumor of the pineal body. The diagnosis was accurately made from the roentgenograms of the skull.

CASE 8.—*Calcareous masses in an ependymal glioma of the left occipital globe.*

A Mexican girl, aged 6, was admitted to the service of contagious diseases, with the provisional diagnosis of encephalitis. A clear history of the illness was not obtained, but the child had been ill for about a month before coming to the hospital. She suddenly became comatose, and two days later was admitted.

On examination, the child appeared deeply comatose. The left pupil was widely dilated and there was evident weakness of the extra-ocular muscles on the left side. There were no other positive neurologic observations. Lumbar puncture revealed that the spinal fluid was clear and contained 60 lymphocytes per cubic millimeter. There was also a trace of globulin.

The child died before roentgenographic studies could be made.

At necropsy a large multilocular cyst occupying the entire posterior portion of the left hemisphere was found, containing yellow coagulable fluid. A mural nodule about the size of a walnut was situated on the medial wall of the largest cyst. In the central portion of the tumor, large calcareous masses were encountered. These felt like particles of bone and were limited in extent to this single portion of the tumor.

Comment.—This is the only case of an ependymal tumor of the series in which calcareous material was found. It is also of interest to note the situation of the tumor in the left occipital region. It probably had its origin from ependymal rests derived from the posterior portion of the lateral ventricle. Van Dessel also reported a case of ependymal tumor in which calcification had occurred.

CASE 9.—*Calcification in an invasive neurogliablastoma multiforme of the left frontal lobe.*

A housewife, white, aged 38, was admitted to the service of Dr. Carl W. Rand at the Good Samaritan Hospital. She gave a history of right-sided convulsive seizures of five and one-half years' duration, associated occasionally with periods of unconsciousness. The condition grew steadily worse, so that in recent months the patient had difficulty with speech following the convulsive seizures.

On examination the patient appeared rather nervous and emotionally unstable. The eyegrounds showed filling of the optic cups and a fulness of the retinal veins. There was a definite weakness of the right arm and leg associated with an increase in the deep reflexes, a Babinski sign and ankle clonus on that side. There was also a decrease in sensation on the entire right side of the body.

Stereoscopic films of the skull did not reveal any evidence of intracranial calcification.

A diagnosis of left frontal tumor was made, and an exploration revealed an invasive glioma of the left frontal lobe which was only superficially resected. The patient died a few days later.

The brain was removed by Dr. Roy W. Hammack, pathologist to the Good Samaritan Hospital. There was an extensive infiltrative, poorly delineated glioma of the left frontal lobe which seemed to originate from the anterior portion of the corpus callosum, spreading into the left hemisphere. Histologic studies showed it to be a neurogliablastoma multiforme with very small calcareous particles in its margin and in the adjacent brain tissue.

Comment.—This case is interesting in that it had a long course for the type of tumor found at necropsy. The small particles of calcareous material failed to be visible in the roentgenograms of the skull as in two

Fig. 6 (case 11).—Solid calcified mass in a presumed glioma of the left parietal region.

of the previously reported cases. Of special interest was the fact that most of the calcification occurred in the adjacent part of the brain rather than in the tumor itself.

CASE 10.—*Calcification in a fibrillary astrocytoma of the right cerebellar hemisphere.*

A boy, aged 10, came under the care of a private physician, Dr. Dee M. Rees, who furnished us with a history of the case and with the pathologic specimen. Four years prior to his present illness, the patient had a period of severe headaches associated with vomiting and obstinate constipation. After an illness of four months the symptoms cleared up, and, aside from slowness in learning at school, the child seemed to be normal. In October, 1929, there was a recurrence of the headaches which seemed to have a fronto-occipital situation and which

were again associated with vomiting. He developed a ravenous appetite, which, together with alternating constipation and diarrhea, led numerous observers to make a diagnosis of intestinal worms, for which he was treated.

On examination, the child appeared somewhat emaciated and not very alert. The forehead seemed more prominent than usual, and the entire head was enlarged. The pupils were dilated and equal and reacted sluggishly to light. There was a lateral nystagmus, particularly to the left. All the deep and superficial reflexes were abolished. The limbs were rigid, particularly the lower extremities, the neck was stiff, and there was a positive Kernig sign on the left side.

The child died shortly after coming under the observation of the referring physician and before roentgenographic studies could be made.

At necropsy, the brain was found to be much congested, the convolutions flattened and the lateral ventricles much dilated with clear fluid. In the right cerebellar hemisphere was a firm, fairly well delineated tumor, about 4 cm. in diame-

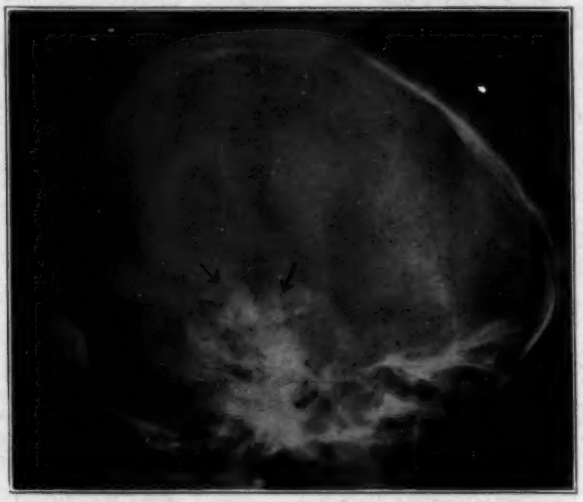

Fig. 7 (case 12).—Solid mass of calcification in a possible slow growing glioma of the left temporal lobe.

ter, with central softening. About the softened area were numerous calcareous particles which gave a gritty feel to the cut surface of the tissue. The peripheral portion seemed to be free from calcification.

The heart and lungs appeared normal on gross examination, the bowel was much thickened and its lumen gave evidence of chronic inflammation. The thymus was enlarged and the lymph nodules were generally hypertrophied.

Comment.—This case is unusual in that it is the only one in the series in which a tumor was situated beneath the tentorium. Tumors in the posterior fossa, because of their tendency to cause hydrocephalus, probably bring about death before calcification takes place, even though they are essentially benign and of slow growth. It is likely that in this case the tumor had begun its course four years previously, and for some unknown reason had become quiescent and had undergone calcareous

degeneration. With a resumption of its growth activities, there was a recurrence of symptoms which brought about the death of the patient. As far as we have been able to determine, there has been no other case reported in which a calcified glioma was found in the posterior fossa.[42] It is to be regretted that no roentgenographic studies were made.

UNVERIFIED CASES

The following cases are described because of the special interest of the clinical history and the roentgenograms of the skull even though the tumors were not verified histologically. Van Dessel and Fraenkel

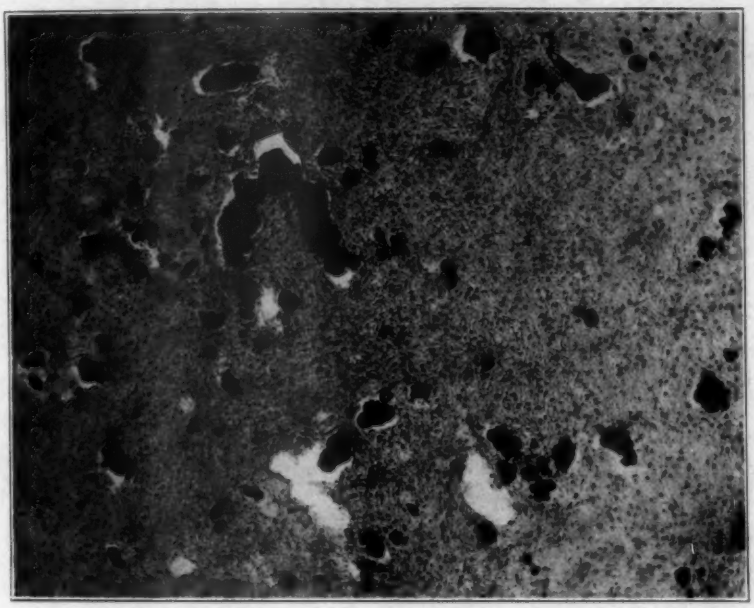

Fig. 8 (case 5).—Calcareous masses scattered more or less evenly throughout the tissue of the tumor. Hematoxylin and eosin; × 95.

mentioned the occurrence of calcification within the walls of gliomatous cysts, the former author reporting two which were evacuated at the time of operation. We are unable to say whether these tumors were solid or cystic, because they were deep within the substance of the hemisphere.

42. In 1899 Church reported a case of cerebellar tumor which he claimed to have demonstrated by the roentgen ray. This has not met with universal acceptance because the glioma exposed at necropsy did not contain calcium and, from the roentgenogram shown in his article, it is doubtful if the opaque area represented the tumor (Church, A.: Cerebellar Tumor Recognized Clinically, Demonstrated by the X-Ray and Proved by Autopsy, Am. J. M. Sc. **117**:125 [Feb.] 1899).

CASE 11.—*Calcification in a presumed glioma of the left parietal region.*

A Mexican girl, aged 15, was admitted to the neurologic service of the hospital on Jan. 28, 1929. She complained of headaches, vomiting and progressive failure of vision of one and one-half years' duration. During this period she had two convulsive seizures of a generalized character.

When first examined, the patient was completely blind. The pupils were widely dilated and reactionless. A bilateral primary optic atrophy, more marked on the left side, was present. There was a complete right hemiparesis associated with increased deep reflexes, ankle clonus and a Babinski sign on that side. Sensation was also diminished on the right side, and a suggestive astereognosis of the right hand was noted on repeated examinations.

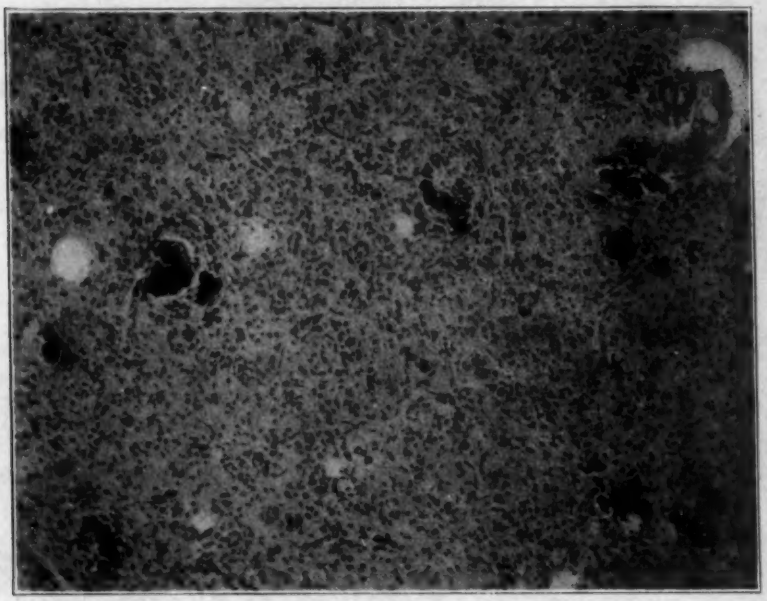

Fig. 9 (case 7).—Localized masses of calcification scattered throughout the tumor tissue. Hematoxylin and eosin; × 180.

Stereoscopic films of the skull revealed a small, rather sharply defined area of calcification deep in the left parietal lobe (fig. 6).

On June 30, a left osteoplastic bone flap was laid down, but no tumor was seen superficially. The patient's condition was poor, and the operation had to be concluded. The patient's family refused to consider further operative procedure, and she was discharged after an uneventful recovery. She returned on several occasions to the clinic but there was no further change in her condition, except for some bulging of the decompression area.

Comment.—It is to be regretted that tissue could not be recovered from the lesion to verify the diagnosis. The growth was probably a deeply seated, slowly growing glioma.

CASE 12.—*Calcification in a possible glioma of the left temporal lobe.*

A Mexican woman, aged 27, was transferred from the otorhinolaryngology service of the hospital. She had been under observation for acute frontal and maxillary sinusitis, having complained of pain in the left side of the head associated with generalized convulsions for three years. A right hemiplegia of gradual onset had been present since the age of ten.

Examination disclosed a marked right-sided hemiplegia, associated with an increase in the deep, and a decrease in the superficial, reflexes. A definite Babinski sign was present on the right side and a suggestive one on the left. Perimetric examination demonstrated the presence of a right homonymous hemianopia.

Stereoscopic films of the skull showed a compact mass of calcification in the region of the left temporal lobe (fig. 7).

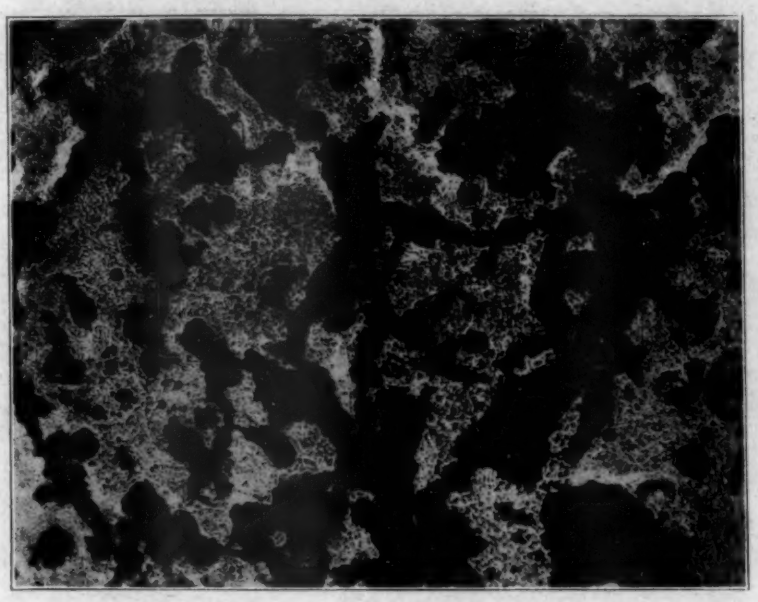

Fig. 10 (case 10).—Masses of calcareous material in the central portion of a cerebellar astrocytoma. Hematoxylin and eosin; × 95.

A left osteoplastic flap was turned down on July 11, 1928. The calcareous mass could be palpated through the overlying cortex, but owing to the patient's poor condition, a decompression opening was made and the wound closed. The patient made an uneventful recovery and was well when last examined.

Comment.—This case also lacks positive verification of its true nature. Because of the left-sided headaches, the homonymous hemianopia and the right hemiplegia of slow onset, we assume that it was a neoplasm, possibly a glioma.

THE PROCESS OF CALCIFICATION IN THE GLIOMAS

The deposit of calcium within the body tissues is dependent on some chemical change which favors the precipitation of blood calcium. The

calcium salts of the blood are held in simple solution or in combination with protein substances. This suspension or combination, evidently an unstable one, may be altered by variations in the hydrogen ion concentration of the tissues, changes in the carbon dioxide tension, or perhaps by qualitative or quantitative changes in the salts themselves, as was suggested by Wells.[43] This author further believes that necrosis, hyaline change and an enfeebled circulation are also factors in the process. It is also possible that such regressive changes in the involved tissue result in the formation of some calcium-binding substance, such as phosphoric acid or the fatty acids. This is significant in view of the occurrence of

Fig. 11 (case 1).—Bone formation in a neurogliablastoma multiforme of the corpus callosum. Hematoxylin and eosin; × 95.

calcium deposit in those parts of the glioma which have undergone a degree of fibrosis.

The necessity of this predisposing degenerative process was accepted by van Dessel in his study of calcification in the gliomas. He observed the presence of hyaline changes in the walls of blood vessels in which calcium was deposited. This is in accord with the view of Mallory,[41] who considered hyaline change in the blood vessels as necessary for the deposition of calcareous material. In our cases, we were struck with the almost complete absence of hyaline change; there was very little

43. Wells, H. G.: Chemical Pathology, Philadelphia, W. B. Saunders Company, ed. 5, 1925, p. 486.

evidence of any other type of regressive process. As previously stated, the calcareous masses were inclined to be more common in areas where a certain degree of fibrosis had taken place. Whether this is a coincidental or an associated observation is not possible to settle at this time. In a few instances minor hyaline changes in the walls of the blood vessels, as indicated by a loss of tissue morphology, were observed but never to the degree described by van Dessel. From our observations it seems evident that the essential factor must be an interference with local tissue respiration which may take place without any alteration in tissue structure.

The distribution of the calcareous particles within the gliomas varied greatly in the different cases as observed under low power magnification.

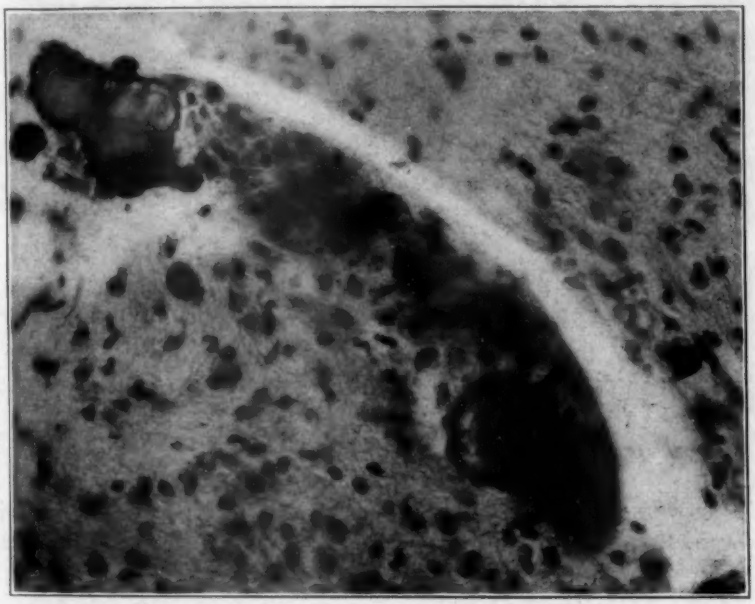

Fig. 12 (case 5).—Colloid globules in the wall of a blood vessel in which calcification is taking place. Hematoxylin and eosin; × 350.

In some instances, it was fairly evenly distributed throughout the tumor tissue (figs. 8 and 9); in others, it was bunched together or confined to one or two larger masses in a single situation (fig. 10). In one glioma, a large central mass proved to be actual bone (fig. 11).[44] This irregu-

44. Actual bone formation in tumors of the intracranial structures is apparently of very rare occurrence. The only cases that we have found cited in the literature are those referred to by Oppenheim—a partly ossified tumor of the cerebral hemisphere and bone formation in a glioma (Oppenheim, H.: Die Geschwülste des Gehirns, ed. 2. Nothnagel: Handbuch der speziellen Pathologie, 1903, quoted by Schüller [footnote 1]).

lar distribution accounts very likely for the comparatively low percentage of calcified gliomas found at operation, the calceroeus particles being situated in the remaining deeper portions of the tumor. In the neurogliablastomas of our series, the more cellular and rapidly growing portions contained no calcium, while the more fibrous and acelluiar areas were studded with calcretions.

The calcification was found most characteristically in the adventitia or media of the blood vessels. In no instance was it found in the intima, although droplets of calcium were observed on one occasion within a group of blood cells within the lumen. The situation of the deposit would suggest that the process rarely takes place in actual con-

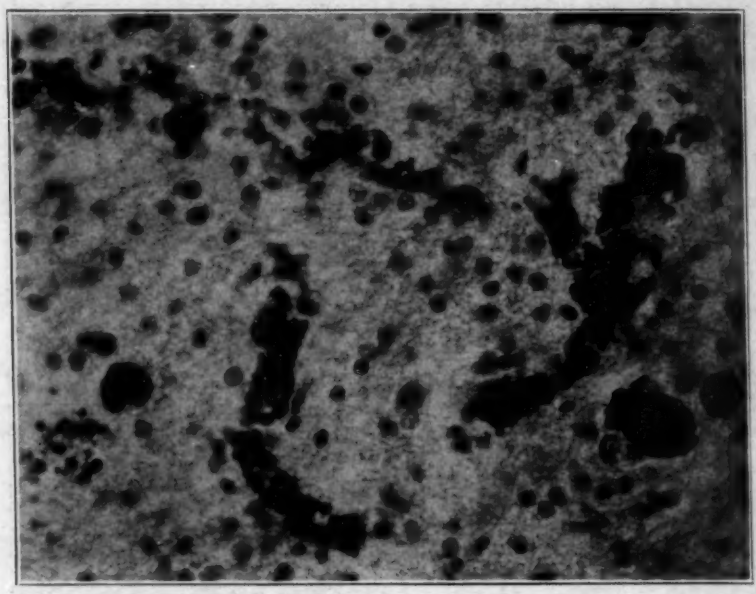

Fig. 13 (case 5).—Spotlike calcification marking the course of capillaries in the margin of the glioma. Hematoxylin and eosin; × 350.

tact with the circulating blood, but rather in tissues somewhat removed from it. It also suggests that calcification usually is not primary in the tissue where an active circulation of the tissue fluid is taking place, but that in these areas it is usually secondary and spreads outward from the vessel.

The preliminary stage in the process, at least in the larger vessels, was the appearance of small round, shotlike globules in the media (fig. 12). Mallory [45] referred to the presence of these droplets which precede the actual deposit of calcium and considered them to be of a colloid nature. In the smaller vessels and capillaries, the droplets of calcareous

45. Mallory, F.: A Contribution to the Study of Calcareous Concretions in the Brain, J. Path. & Bact. **3**:110, 1896.

Fig. 14 (case 5).—Calcification of the wall of the blood vessel forming a ring. The lumen is also occluded. Hematoxylin and eosin; × 350.

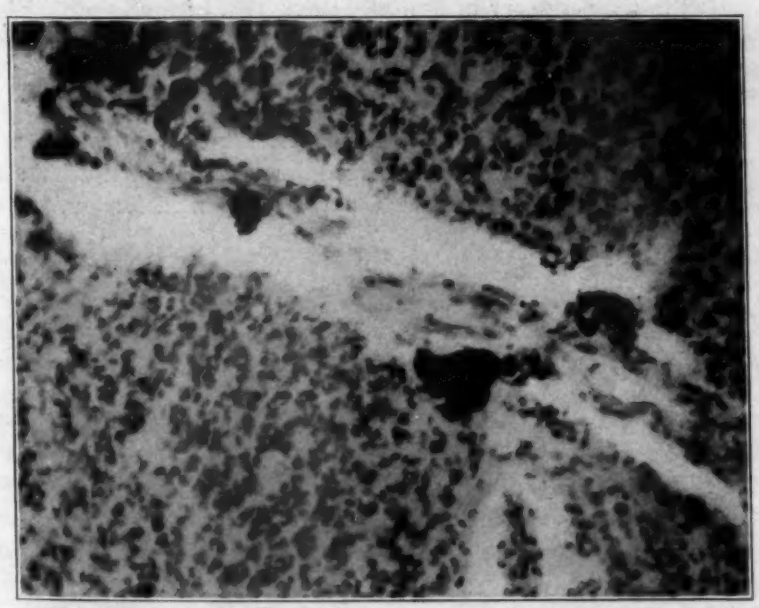

Fig. 15 (case 7).—Masses of calcareous material in the adventitia of a small blood vessel. Hematoxylin and eosin; × 220.

material appear as round individual or coalesced globules which marked the course of the involved vessels through the tissue (fig. 13). In a further stage, coalescence of the globules converts the vessel into a rigid tube best seen in cross-section as a ring of calcium (fig. 14). Complete occlusion of the lumen may follow. In the smaller vessels, where distortion may take place easily, the lumen may be obliterated early, appearing as a small solid mass of calcareous material. Where some of the larger vessels have been sectioned longitudinally, small masses of calcium are observed here and there in their course (fig. 15). In our case of calcification in an ependymal glioma, the calcified vessels formed a veritable meshwork in a central fibrosed area (fig. 16). This is suggestive of the process described by Bassoe and Hassin.[46]

In one case, small shotlike particles of calcareous material were found scattered throughout the tissue, having no particular relationship to its vasculature. In this case, corpora amylacea were observed, some of which were undergoing calcification (fig. 17).

The process occurs less frequently and characteristically within individual tumor cells. Either the nucleus or the protoplasm of the cell may be the seat of small globules of calcium. Whatever the original situation may be, it tends to expand peripherally so that the entire cell is filled with a spherical mass. When starting in the protoplasm, which seems to be the more common point of origin, the nucleus is found crowded to the periphery of the cell in the form of a crescent. When the process occurs in a group of cells, it gives the appearance of a bunch of grapes (fig. 18).

The deposit of calcium in the stroma as a primary process was unusual. We observed it in a few isolated places in which small globules were found outside of a cellular structure and within the fibrillary stroma. This phenomenon may be accounted for by the comparatively less demand for active metabolic activity on the part of the stroma. Calcium was found in a few instances within extravascular masses of blood cells.

The association of calcification with small cystic cavities at the margin of slower growing neurogliablastomas was observed in two cases. The cysts are probably the result of tissue liquifaction incident to an interference with the local blood supply. In the cases studied, the calcareous particles were confined to the margin of the tumor and the adjacent brain tissue, none being found in its more central portions. The small particles were found largely in the walls of the capillary blood

46. Bassoe, P., and Hassin, G. B.: Calcification of the Cerebral Vessels with a Clinical Picture Simulating Brain Tumor, Arch. Neurol. & Psychiat. **6**:361 (Oct.) 1921, figure 2.

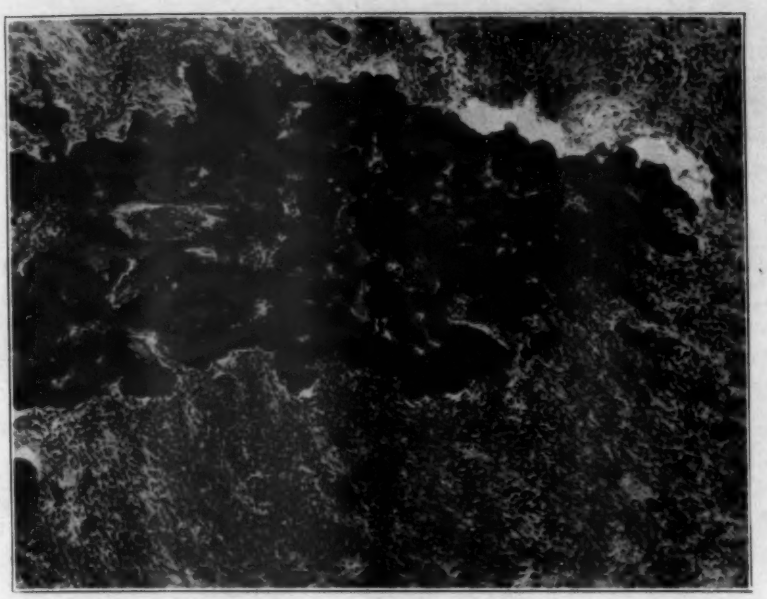

Fig. 16 (case 9).—Meshwork of calcified blood vessels in the central portion of an ependymal glioma. Hematoxylin and eosin; × 95.

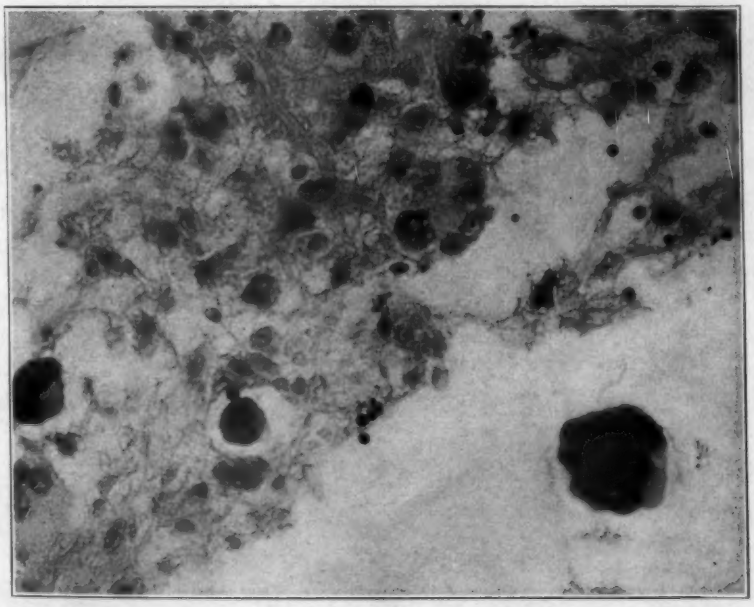

Fig. 17 (case 3).—Calcification occurring in a corpus amylacea. Spotlike calcifications are also seen scattered throughout the tissue. Hematoxylin and eosin; × 700.

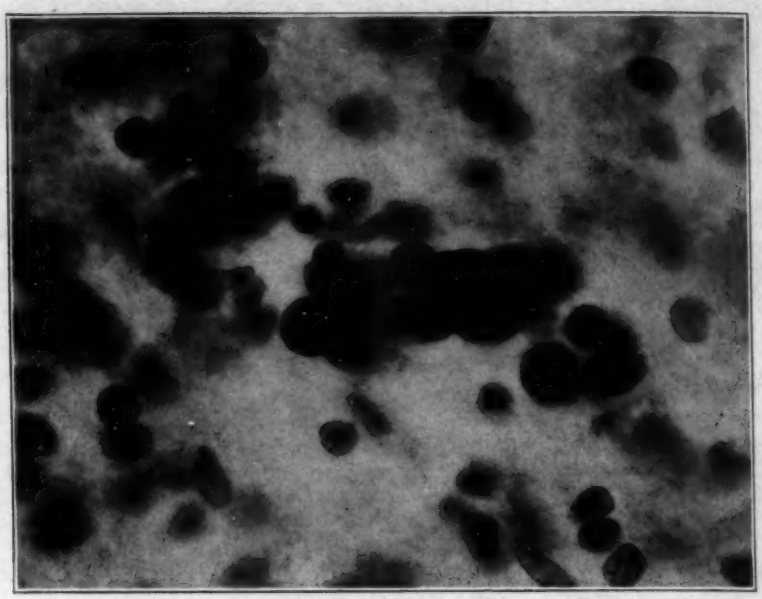

Fig. 18 (case 7).—Calcareous degeneration taking place in a group of tumor cells. Hematoxylin and eosin; × 885.

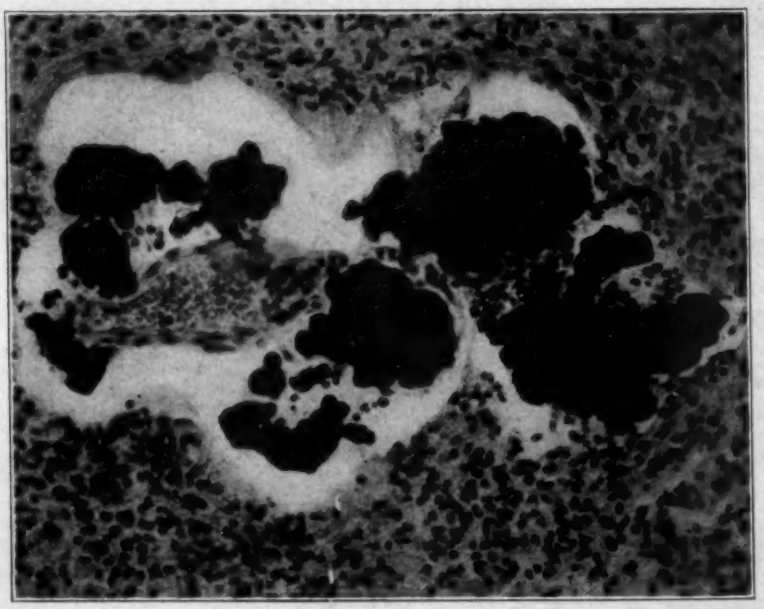

Fig. 19 (case 7).—Showing the relation of the calcareous masses to a blood vessel. Hematoxylin and eosin; × 220.

vessels. Its small bulk was further emphasized by the fact that a review of the roentgenograms showed no evidence whatever of its presence. Whenever the margin of the tumor appears spongy in the gross specimen, it is possible that such calcareous deposits will be found. This seemed to be the case in a glioma of this type studied by Medakovitch.[38]

In the brain tissue at the margin of the tumor in our cases, the process seemed to be confined entirely to the walls of the blood vessels. Careful study of the ganglion cells undergoing regressive changes revealed no deposit of calcium. We interpreted this to mean that the degenerative process was taking place too rapidly or that the other factors were absent. Landau[47] reported the occurrence of spotlike calcification in the blood vessels and the ganglion cells at the margin of a diffuse glioma.

A review of the question of calcification within the tissues of the brain shows that numerous conditions may bring about an alteration of the respiratory exchange favoring the deposit of calcium. This change seems to affect most characteristically the walls of the blood vessels, but may extend out to involve the elements of the nervous system. In this sense a glioma may be considered as one of the factors that interfere with the respiratory activity to the extent that calcium is deposited. This is true particularly when it is recognized that the blood vessels of the glioma are probably those of the preexisting brain tissue the space of which the tumor has come to occupy, although some are also newly formed. Strength is added to the argument by the deposit of calcium in the marginal brain tissue, often in addition to that in the glioma itself, the nutritional disturbance extending for a variable distance beyond the actual borders of the tumor.

SUMMARY AND CONCLUSIONS

1. A short general review of the occurrence of intracranial calcification is given, with the pathologic possibilities. Calcareous deposit may be found in practically every type of primary intracranial new-growth, although with the exception of the craniopharyngeal pouch cysts it is probably most common in the gliomas.

2. Hyaline degeneration or other marked regressive changes are not essential to the deposit of calcium in gliomas. It is essentially a chemical rather than a histologic process. The calcareous material is found characteristically in the media and the adventitia of the blood vessels, occurring to a much less extent in the cells of the tumor and very rarely in the stroma. The association of calcification in small blood vessels with liquefaction cysts at the margin of the glioma is noted.

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47. Landau, Max: Das diffuse Gliom des Gehirns, Frankfurt. Ztschr. f. Path. 5:469, 1910.

3. The presence of calcification is of value in the diagnosis and localization of gliomas, and further emphasizes the importance of securing satisfactory roentgenograms of the skull in every case in which intracranial tumor is suspected. The distribution of the calcareous material is usually evenly spread throughout the tumor tissue and gives some conception as to its size and relationships. The duration of the symptoms will often suggest the type of glioma that can be suspected; those with a history of from six to twelve months will likely be neurogliablastomas (spongioblastomas), while those of longer duration will more likely be astrocytomas.

4. Because of the small size of the individual masses, calcareous material may be present in a glioma and yet fail to appear in the roentgenogram. Roentgen examination usually reveals an associated thinning of the skull over the tumor, indicating a local rather than a general increase in pressure.

5. As observed either roentgenographically or histologically, the calcareous particles show a variable distribution in the tumor tissue. They may be spread evenly or unevenly throughout the tumor or may be confined to a single dense mass in its more central portions.

6. Calcification in a glioma is an indication of its relative rather than its absolute benignity. A large proportion of our cases showed the variety of glioma considered malignant. The process may apparently occur in any type of the group.

7. Twelve cases are reported. Of the ten growths verified histologically, five proved to be neurogliablastomas (spongioblastomas), three were astrocytomas, one was an ependymal glioma (ependymoblastoma) and one an unclassified glioma, apparently a cerebral medulloblastoma.

8. Actual bone formation was found in one case. In the literature we found the record of but one other case in which bone formation had taken place in a glioma, that of Oppenheim. We report a case of calcification in a cerebellar glioma, the counterpart of which we have not been able to find in literature. This is probably of more relative than actual import, for there is no reason why calcification should not occur in the cerebellar astrocytomas, unless the early production of hydrocephalus brings about the patient's death before the process takes place.

Dr. Ray A. Carter, head of the Department of Roentgenology of the hospital, permitted us to use the roentgenograms shown, as well as his valued reports.

THE CLOSED INTESTINAL LOOP

I. RELATION OF INTRALOOP (JEJUNUM) PRESSURE TO THE CLINICAL CONDITION OF THE ANIMAL *

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This work was undertaken in an attempt to throw further light on the relation of hydraulic pressure within infected hollow viscera to the clinical course presented. It was pointed out by Van Zwalenburg [1] that as the distention of hollow viscera takes place by increased pressure from within, the circulation is gradually blocked and effusion into the lumen tends to increase the fluid and pressure there. Necrosis and rupture are the natural sequelae. In most instances the viscus contains many organisms and toxic products which when freed by rupture spread infection and permit of wide surfaces for absorption, resulting in death.

It seemed to us that the closed intestinal loop in the dog, as introduced by Whipple [2] and his associates, if placed where it was accessible for measuring the intraloop pressure without adding complications to the situation, should lend itself admirably to this investigation. Accordingly, the following procedure was used in preparing the animals for this study:

EXPERIMENTAL PROCEDURE

Entering the peritoneal cavity through a right rectus incision, we chose a segment of jejunum with a good mesenteric blood supply which would not be embarrassed when sufficient tension was placed on it to bring the segment to the anterior abdominal wall. The distance of such a segment from the ligament of Treitz varied in different dogs but averaged about 25 cm. In the early experiments we attempted to make the loop approximately 20 cm. from the ligament of Treitz.

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* From the Department of Physiology, University of Oregon Medical School.

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1. Van Zwalenburg, C. V.: Strangulation Resulting from Distention of Hollow Viscera, Ann. Surg. **46**:780, 1907.

2. Stone, H. B.; Bernheim, B. M., and Whipple, G. H.: Intestinal Obstruction: A Study of the Toxic Factors, Bull. Johns Hopkins Hosp. **23**:159, 1912.

In some dogs this resulted in a strangulated loop so that such a criterion for its location was abandoned. The length of the segment, too, varied with its mesenteric supply but averaged about 15 cm. After the ends were turned in and the loop had contracted from trauma, it was considerably shorter. A very fine curved intestinal needle and 00 plain catgut were used in closing the ends. Ample inversion (1 cm.) was made in order to prevent the end from opening on early postoperative rise of intraloop pressure. The loop was then dropped back into the peritoneal cavity and the continuity of the gastro-intestinal tract reestablished by an aseptic, end-to-end anastomosis. This accomplished, the midline fatty

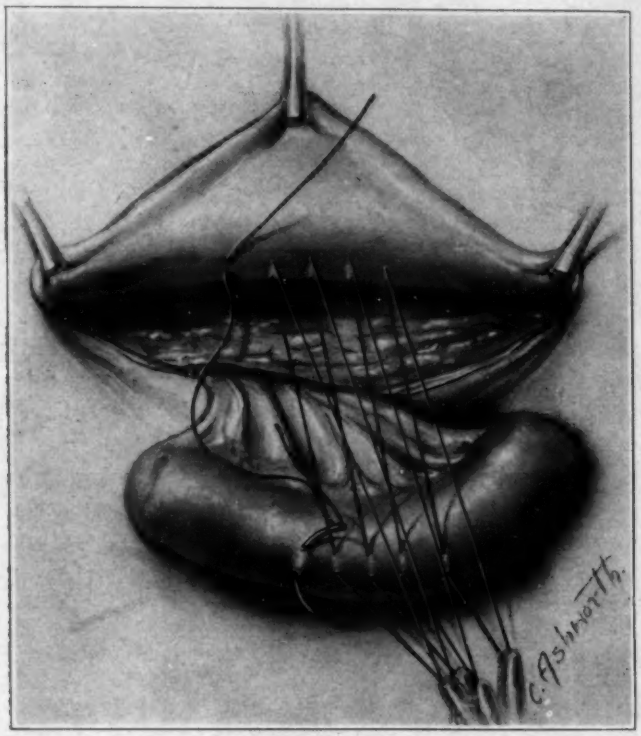

Fig. 1.—The sutures placed for attaching the loop to the anterior abdominal wall.

appendage was dissected back over the midline between the xiphoid process and the umbilicus, giving a traumatized area to which the loop was attached in its midthird portion. Suturing here was done with 0 silk on a very fine curved intestinal needle. Interrupted sutures were used which were passed first through the peritoneum and then through the antimesenteric portion of the intestinal wall. In placing this intestinal stitch, we made no attempt to pick up the submucosa. If the submucosa was engaged, it was only in its outermost zone. This is, of course, contrary to good intestinal surgical technic in that it is the submucosa that can withstand the pressure of suture tension. However, in the dogs used in the earlier part of the experiment we found that loop perforation from pressure often occurred at the site of one of these sutures. This may well have been due to placing the

sutures too deeply, even into the mucosa. Since we have been making a studied attempt to pick up no more than the outermost layer of the submucosa, we have had no perforations at the point of suture. The sutures were all placed before they were tied as shown in figure 1. When the operation was complete, the jejunal loop was held against the anterior abdominal wall as shown in figure 2, and two linen sutures were placed in the skin of the anterior abdominal wall to show the midpoint of the loop attachment. Closure of the right rectus wound was done by the usual three-layer suture method. These loops almost uniformly adhered to the abdominal wall, so that the loop could be punctured at will for the study of loop contents.

After operation, the dogs were kept in separate cages in a warm room. Water was given after forty-eight hours, and milk or hamburger after ninety-six hours. Approximately twenty-four hours following the operation the dog was placed on the operating table and the skin over the area of attachment of the loop cleaned with alcohol. A hypodermic needle (no. 19) was then inserted through this area into the loop. Attaching a sterile syringe, the operator first made sure that

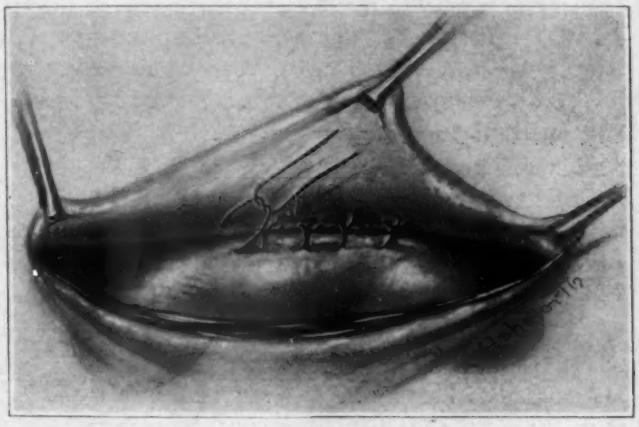

Fig. 2.—Loop attached to the anterior abdominal wall.

the needle was in the loop and the fluid free to flow out. The syringe was then removed and a sterile apparatus attached for measuring the pressure in the loop. This consisted of a straight piece of glass tubing of 3 mm. bore and 35 cm. long, to which a rubber tube 24 cm. long was attached. The quantity of fluid removed from the loop in measuring the pressure was thus at no time sufficient to affect the pressure materially. After the pressure was determined, the fluid was withdrawn with the syringe. This procedure was usually repeated each day for the first three or four days. Evidence thus gained as to the rate at which the fluid formed was used in deciding whether or not "tapping" should be continued at regular intervals.

Fifty-one dogs were used in this study of the jejunal loop. Twenty-three of these died within ninety-six hours. At autopsy, the causes of death were divided as follows: Three had peritonitis from an imperfect end-to-end anastomosis; four had rupture of the loop at one of the stitches used to hold it to the abdominal wall; one died as a result of

anesthesia and three from respiratory infection; three had no fluid removed from the loop, with consequent rupture and peritonitis; nine died in spite of the removal of fluid, owing to the fact that the mesenteric vessels were compressed at the root (strangulation). This, we discovered, after several animals had been lost, could be avoided by choosing a loop lower down in the jejunum. Because of differences in the mesenteric root in different dogs, it became necessary to study the mesentery of a segment to make sure that tension on it (as when brought to the anterior abdominal wall), did not embarrass the circulation at the root.

Sixteen animals were lost in less than thirty days following the operation. Some of these were not tapped for several days before death. The loop had become distended and ruptured before any objective symptoms were noticed. In a few animals gangrenous loops developed in spite of tapping, probably due to embarrassment of the circulation at the root of the mesentery. Three were lost because of infection in the incision; two showed peritonitis due to imperfect end-to-end anastomosis, and one died on the fifth day from ruptured loop, no fluid having been removed at any time.

Of the remaining twelve dogs, three were killed for histologic examination of the loops, three are alive and six died from ruptured loops. The average length of life of this group was more than four months.

COMMENT

As is seen from the foregoing description, there are several possibilities for complications. To those enumerated should be added the experimental hazard of tapping the loop. One can miss the loop easily if it is contracted, or the needle, if too long, may go through the loop and carry organisms into the peritoneal cavity. If there has been only a narrow adhesion of the serosa of the loop to the anterior abdominal wall, the needle may miss this area and enter the loop on its free surface. This again furnishes a possible source of contamination of the peritoneal cavity.

We feel, therefore, that, barring the experimental difficulties of the various types mentioned, the simple expedient of keeping down the intraloop pressure is the outstanding factor in the recovery of these animals. At this level in the intestinal tract pressure develops in the closed loop on the first or second day after operation. This may continue for several days, even with withdrawal of fluid. It was found necessary in most dogs to withdraw fluid every few days during the life of the animal.

The amount of pressure found in the closed loops varied from 0 to 56 cm. of water. The highest pressures recorded the first few days

following the operation are taken as indicative of the intraloop pressure that might be effective in blocking the circulation. As a result of operative trauma, the tone of the muscularis is greatly decreased and a pressure that would cause little distention normally is now capable of causing marked distention. This combines two factors in producing circulatory stasis, namely, intraloop pressure and stretching of the capillaries. A loop markedly distended by a pressure of 25 or 30 mm. of mercury has its circulation partially blocked. This is evidenced by necrosis on the antimesenteric border of the loop. In the accompanying table are recorded the highest pressures found in fifteen dogs the first few days following operation. The average high pressure is 39.5 cm. of water or 30.4 mm. of mercury. One would expect this to be

The Highest Intraloop Pressures Recorded Together with the Amount of Fluid Removed from the Loop*

Dog	Pressure, Cm. of Water	Quantity of Fluid Withdrawn, Cc.	Days Following Operation	Length of Life Following Operation, Days
4	45	50	3	24
6	32	60	2	8
9	30	45	9	96
10	38	51	3	9
11	26	20	2	4
12	30	45	6	174
23	45	55	4	50
34	45	90	2	2
36	42	90	1	4
37	42	75	3	4
38	36	50	2	5
40	46	105	3	4
43	52	35	3	11
44	56	95	3	4
45	28	50	4	4

* The average loop pressure was 39.5 cm. of water.

below the pressure required to block completely the circulation to the loop. In most instances the pressure probably was taken before it had reached a maximum, and in others a small rupture had probably taken place and part of the fluid escaped into the peritoneal cavity, thus lowering the pressure.

In this connection Dragstedt [3] and his co-workers recently studied the amount of pressure necessary to block the circulation in a loop of intestine with the dog under anesthesia. They found this to vary with the level of the loop. In the duodenum from 35 to 40 mm. of mercury was sufficient; in the jejunum and ileum from 55 to 65 mm., and in the colon, 95 mm. These were acute experiments, and under such circumstances the actual distention of the loop is not great, owing to the effective resistance of active muscularis. In other words, the

3. Dragstedt, C. A.; Lang, V. G., and Millet, R. F.: The Relative Effect of Distention on Different Portions of the Intestine, Arch. Surg. **18**:2257 (June) 1929.

stretching of the capillary hardly enters into the problem. This, we feel, is a factor in explaining the wide difference between our observations and those of Dragstedt.

Owings, McIntosh, Stone and Weinberg,[4] by using a tube in one end of an isolated loop and allowing the other end of the tube to protrude through the abdominal wall to which it was clamped, investigated the development of pressure in the loop. They obtained a pressure in duodenojejunal loops of 50 cm. of water at the end of twenty-four hours. Only four dogs were used, and these survived from twenty-nine to fifty-four hours.

The clinical symptoms in our dogs in which a closed loop had been made were not marked when the pressure was kept down and the loop did not rupture. Where there were no complications the symptoms were little if any different from those seen in our control animals following intestinal resection and an end-to-end anastomosis of the jejunum. The temperature ranged between 101 and 103 F. There was usually no vomiting and no marked changes in the blood chemistry.

Toxic material from bacterial action is present in the loop in varying amounts at all times. When the loop is not distended and the circulation to it is good there can be very little absorption of this material, or the amount absorbed is detoxified by the liver. Such animals do not differ from normal animals in any demonstrable way, in actions, appetite, temperature or blood chemistry. On the other hand, when the loop becomes distended, objective symptoms are usually present. The dog may have eaten heartily in the evening and twelve hours later may refuse food. The temperature may or may not show a slight rise. The animal is not quite so lively. Of these symptoms the only reliable one is refusal of food. If the animal is tapped, so that pressure is relieved, he may eat at once; if not at once, always within the next hour. A more severe or longer continued distention produces more marked symptoms such as vomiting and depression. On tapping such dogs a large quantity of fluid is found. They are somewhat slower to take food but do so in the course of two or three hours. Even at this time there are usually no significant changes in the blood. If the loop is perforated under this tension, depending on the amount of fluid escaping and its toxicity, the symptoms are slight or the animal shortly becomes moribund. This tendency for a loop to fill with fluid at irregular intervals is seen in most dogs. Tapping may not have been done for several days or weeks, when suddenly the animal refuses food, indicating a distended loop. This may occur every day or every other day for a week or ten days, when the fluid gradually ceases to form

4. Owings, J. C.; McIntosh, C. A.; Stone, H. B., and Weinberg, J. A.: Intra-Intestinal Pressure in Obstruction, Arch. Surg. **17**:507 (Sept.) 1928.

faster than absorption takes place. The cause of these periodic disturbances in the secretion absorption balance in the loop is not clear. Although it is possible that the disturbance is brought about by irritation from within, it seems more probable that it is due to pressure on the mesenteric vessels by an over distended colon, and that the fluid results from filtration rather than from secretion.

These attacks, even though the animal may have vomited several times, are probably due more to reflex nausea and pain from the distended loop than to absorption of toxic products. This theory is borne out by the facts that (1) at this time the blood chemistry shows little or no change and (2) the animal eats either at once or within two or three hours, all objective symptoms having disappeared.

The flora more or less regularly found in these loops include *Bacillus coli, Bacillus welchii* (organisms and spores), enterococci and streptococci. Other organisms have been found but less regularly and in smaller numbers. As the loop becomes older, *B. welchii* disappears and one of the other three types tends to predominate. It seems clear that only a slight inhibitory influence is exerted by the secretion of the loop on its bacterial content. Those organisms that can thrive on the mucus and débris in a slightly alkaline medium battle for predominance. There is some evidence that great numbers of organisms, when present, may directly or indirectly cause excess formation of fluid. The rôle of organisms is being carefully studied.

Different investigators have been led to believe that the hydrostatic pressure in closed loops of intestine is an important factor in determining the clinical course of the animals. Sweet, Peet and Hendrix [5] stated the opinion, "that it is only because of such distention and consequent rupture that our animals with closed loops die." Dragstedt [6] and his associates showed that dogs with closed loops washed with astringents would live indefinitely. They made the following statement: "The factor of distention in short closed intestinal loops is of paramount importance in the production of the toxemia, since if the distention is prevented in the majority of cases toxemia does not occur." More recently Dragstedt [7] stated: "The toxemia and decrease in blood chlorides is in turn dependent upon distention of the closed intestinal segment. If this distention is relieved by aspiration of the fluid within

5. Sweet, J. E.; Peet, M. M., and Hendrix, B. M.: High Intestinal Stasis, Ann. Surg. **63**:720, 1916.

6. Dragstedt, L. R.; Dragstedt, C. A.; McClintock, J. T., and Chase, C. S.: Intestinal Obstruction: II. A Study of the Factors Involved in the Production and Absorption of Toxic Materials from the Intestine, J. Exper. Med. **15**:109, 1919.

7. Dragstedt, L. R.: Blood Chemistry in Intestinal Obstruction, Proc. Soc. Exper. Biol. & Med. **25**:239, 1928.

the segment, by a needle thrust through the abdominal wall, the toxemia is relieved and there occurs a proportionate return of blood chloride concentration toward the normal level." Stone and Firor [8] tested the absorption of india ink by the intestine below and above a point of obstruction. In the latter instance only were they able to recover it from the mesenteric glands and lymphatics. They also placed a loop of intestine containing toxic material and distended with air, in Ringer's solution. This solution soon showed toxic properties. Raine and Perry [9] concluded that, "diminishing intra-intestinal pressure in an obstructed bowel prolongs the life of rabbits, because it diminishes secretion and promotes reabsorption." When the closed loop is made available, as described by us, it is possible to get more direct evidence as to this relationship. In our experience, hydrostatic pressure develops in practically all closed jejunal loops. The relief of this pressure permits a normal recovery, provided the circulation is good. There is little or no vomiting unless the loop is distended. Decrease in blood chlorides, typical of clinical obstruction, was not seen in our animals.

Dogs 15, 20 and 31 were killed after 178, 160 and 126 days, respectively; all were in excellent condition at this time. Dogs 15 and 20 had been tapped at irregular intervals since the loop was made; neither had been tapped for two weeks preceding their death. Dog 31 had not shown signs of pressure, and no fluid had been removed from the loop since the fifth day following operation. Grossly, these loops appeared normal. A gray pasty-like material was present in the loops; when this was washed away, the mucosa appeared normal. Except for occasional areas which showed absence of the epithelial covering, microscopically, the mucosa appeared essentially normal. Some short and broad villi were present that showed an increased cellular infiltration over that seen in control sections from normal jejunum. The muscularis was uniformly moderately hypertrophied. It is possible that these pathologic changes noted can be accounted for, in part at least, by the accumulated pasty-like material. The needle punctures, also, may have brought about some damage to the mucosa that had not been fully repaired. Histologically, the amount of normal mucosa seen so far exceeded the areas of slight pathologic change that one was led to believe that normal functions of secretion and absorption could be carried on. It would seem, therefore, that such loops might lend themselves to various physiologic or pharmacologic investigations.

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8. Stone, H. B., and Firor, W. M.: Absorption in Intestinal Obstruction: Intraintestinal Pressure as a Factor, Tr. South. Surg. & Gynec. A. **37**:173, 1924.

9. Raine, F., and Perry, M. C.: Intestinal Obstruction: Experimental Studies on Toxicity, Intra-Intestinal Pressure and Chloride Therapy, Arch. Surg. **19**: 478 (Sept.) 1929.

The specimens obtained from the loops were tested regularly for sucrase and erepsin. These observations will be reported later with results in loops at different levels of the small intestine. It should be stated here that the concentrations of these enzymes vary only slightly in a given animal while in good condition. However, if the loop becomes distended with a large amount of fluid, the concentration of enzymes is usually low. This would seem to indicate that in such instances the accumulated fluid may be the result of filtration rather than of secretion.

SUMMARY AND CONCLUSIONS

1. A method of attaching a closed intestinal loop to the anterior body wall where it can be readily reached with a hypodermic needle is described.

2. Dogs with closed jejunal loops, with the continuity of the intestinal tract reestablished, can be kept alive indefinitely, provided the pressure in the loop is kept down by aspiration of the fluid.

3. Such animals with closed jejunal loops, barring complication, do not show the clinical symptoms of obstruction. Vomiting is seldom seen, and the blood chlorides do not undergo significant change.

4. By permitting distention and pressure to take place in the closed loop, vomiting is precipitated; refusal of food is an invariable symptom. The animal is immediately relieved and will eat almost at once following aspiration of the fluid. This would seem to prove that the symptoms are due to reflex nausea and pain from distention of the loop. Although there is probably some absorption of toxins at this time, it is not the important factor in producing the symptoms observed.

5. The flora found in the jejunal loops consists predominately of *B. coli, B. welchii,* enterococci and streptococci.

6. The loops in fully recovered animals appear to be essentially normal and should in some ways be superior to the Thiry fistula for the investigation of problems of secretion and absorption.

SYMPATHECTOMY BY ARTERIAL EXCISION *

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Until the surgeon began to think of bone as a living fabric with qualities other than its hardness and potentialities beyond its mechanics, progress in the rational treatment for diseases and injuries of the skeleton could not proceed. A corresponding total physiologic conception of the peripheral vascular tree has been slow in developing. The peripheral vessels have too long been thought of as more or less elastic tubes of differing calibers, responding only to the mechanical forces developed from the pulse wave and the succeeding elastic recoil. They are not thought of under all circumstances as living structures responding in their own right to nerve impulse as well.

In the light of the rapidly increasing knowledge of the vegetative nervous system, certain aspects of vascular disease are now looked at with a more seeing eye. In Raynaud's disease, the vasospastic elements of thrombo-angiitis obliterans, the vasoconstrictor and vasodilator effects of various physical agents, such as cold and heat, etc., the sympathetic impulse is recognized and made use of in everyday thought and action. The purpose of this paper is to call attention to a factor in vascular disease in which the sympathetic impulse may well play an important part, but in which nerve influence has been somewhat ignored, namely, in the development of a collateral circulation following the obstruction of major vessels.

It is interesting that slight attention has been paid in this country to the possibility of increasing by means of an attack on the sympathetic nervous system the amount of blood passing through collateral channels after arterial ligations. Discussions in the literature of problems of collateral circulation contain no reference to the sympathetic innervation. The Hodgen Lecture [1] of 1929 is an example. In this scholarly and closely reasoned discussion of the effect of ligation of the veins on the collateral circulation following arterial occlusion, Brooks nowhere

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* Read before the Richmond (Va.) Academy of Medicine, Feb. 11, 1930.

* From the Department of Surgery and Gynecology, The University of Virginia School of Medicine, from St. Louis City Hospital No. 1, and from Barnes Hospital, St. Louis.

1. Brooks, Barney: Surgical Application of Therapeutic Venous Obstruction, Arch. Surg. **19**:1 (July) 1929 (The Hodgen Lecture of the St. Louis Surgical Society, Jan. 15, 1929).

makes mention of possible sympathetic influence. Halsted, in 1920,[2] three years after Leriche's first publications[3] on the perivascular sympathectomy of Jaboulay, was the first observer in this country to note possible effects on the collateral circulation of a procedure involving ablation of the perivascular sympathetic. He observed a marked hyperemia of the arm following excision of a large subclavian aneurysm and definitely ascribed this result to the removal of sympathetic fibers with the sac.

Before discussing clinical phases of this problem, it would be well to review briefly present knowledge on the motor innervation of the arteries. Details of sensory innervation, of central connections and of the question of antidromic conduction need not be allowed to cause con-

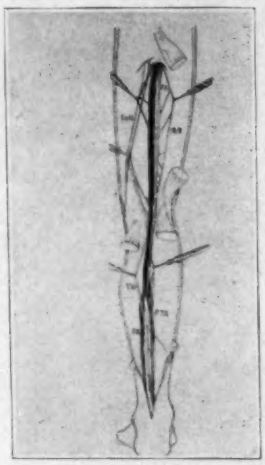

Fig. 1.—Dissection of the lower extremity, showing distribution of nerves to the large arteries. Note that sympathetic branches to the vessel pass from the peripheral nerve to the artery wall at intervals. (Reproduced from Kuntz: The Autonomic Nervous System, p. 138.)

fusion in the present discussion. All blood vessels, including arteries, veins and capillaries, receive sympathetic nerve fibers. These fibers are carried to the vessels in the peripheral nerves and distributed to their walls at intervals along their courses. It has been fairly well shown that few, if any, fibers pass distally from the trunk in the coats of the vessels (fig. 1). The nerves reaching an artery are distributed

2. Halsted: Elevation of Temperature of Hand Following Excision of Subclavian Aneurism, Bull. Johns Hopkins Hosp. **31**:219, 1920.

3. Leriche, R.: De la sympathectomie périartérielle, Presse méd. **25**:513, 1917. Leriche, R., and Heitz, J.: Des effets physiologiques de la sympathectomie périphérique, Compt. rend. Soc. de biol. **80**:66, 1917; ibid., p. 160.

to all coats; the greatest number lie in the adventitia. These, facts in outline, make up the anatomic background for this discussion. Kuntz, in his recent book on the antonomic system,[4] summarizes present knowledge in greater detail.

Over these nerves come impulses from the central nervous system representing the penultimate stage of reflexes and resulting in vasoconstriction or vasodilation. The constrictor influences predominate, so that division of the sympathetic nerve to a part results in vasodilation. Curiously enough, the removal of the adventitial fibers from an artery also results in vasodilation of the entire extremity below the point of attack. This result contradicts the ordinary conception of nerve influence. As I have already remarked, no through fibers are destroyed by this procedure. There is no anatomic basis for predicting any effect whatever, except on the segment of artery from which the plexus is removed. This clearcut paradox, taken with the further fact that experimental reproduction of the phenomenon in laboratory animals has not been accomplished, has done much to retard the general acceptance of Leriche's procedure. The bizarre quality of the reaction is further emphasized by the fact that in isolated instances Leriche has reported vasodilation in the opposite extremity alone, in both the operated extremity and its mate, and, indeed, in all four extremities following periarterial sympathectomy of a single vessel. Again, at times no reaction may occur.

Much theorizing has been done on this subject, but no satisfactory explanation has been proposed. The clinical fact exists, nevertheless, that the stripping of the adventitia from a major artery results in most instances in a striking physiologic sequence: first, the primary effect of a few hours' duration, consisting in intense vasoconstriction to the degree of obliteration of the peripheral pulse, and second, the secondary phase, immediately succeeding, of vasodilation, increased surface temperature and increased volume flow of blood lasting over a period of weeks. This phenomenon has been evoked in a sufficient number of clinical cases to make its recognition sound. No anatomic contradiction can invalidate it. It does not need the support of comparative physiology. The therapeutic effects of the procedure are familiar in certain selected groups of cases, but these are not germane to the present discussion.

Much time has been spent in the laboratory[5] in unsuccessful attempts to reproduce the phenomenon. Leriche[6] proposed a possible

4. Kuntz, A.: The Autonomic Nervous System, Philadelphia, Lea & Febiger, 1929.

5. Lehman, Edwin P.: Periarterial Sympathectomy: An Experimental Study, Ann. Surg. **77**:30 (Jan.) 1923.

6. Leriche, R.: Sur l'étude expérimentelle, etc., de la sympathectomie périartérille, Presse méd. **30**:1105 (Dec. 23) 1923.

explanation. Man, in the course of his development, has needed to compensate for his hairlessness by an increased sensitiveness of his vasomotor mechanism. External changes in temperature do not strike the sensory endings in the skin beneath the thick growth of hair of animals as they do those in the nude skin of man. Man, therefore, has developed a control of his blood vessels more highly specialized and consequently with somewhat different reactions. The discrepancy is explained on phylogenetic grounds. It is an ingenious idea on which it is not necessary, perhaps, to pass critical judgment.

The usual method of removal of the perivascular sympathetics is, of course, the stripping operation on the otherwise intact artery. In selected cases there is an alternative method, namely, the excision of a segment of the whole vessel, the operation of arteriectomy. It is my purpose to present clinical evidence suggesting that arteriectomy in the presence of arterial occlusion has a favorable influence on the distal circulation. If such favorable influence can be shown, the cause of it need not be sought further than in the fact just mentioned. Arteriectomy includes, of necessity, sympathectomy. The reactions shown by the two operations are comparable, differing only in that in the former less blood is available for the dilated vascular tree than in the latter. I propose, more or less tentatively, the excision of a segment of artery in any case of complete arterial occlusion of a major vessel with a view to obtaining a vasodilator effect on the collateral channels. This proposition has been made by Leriche on the basis of early experience in cases of causalgia, trophic change and edema, associated with an obliterated artery. In his later publications,[7] Leriche has carried the proposition still further, including types of disease that I shall subsequently discuss. However, his approach to the problem is somewhat different from that in the present paper. He does not propose to influence the collateral circulation by arterial excision, but rather to excise irritated sympathetic fibers which he believes are creating vasospastic conditions. He therefore takes the position that he is attacking sympathetic disease directly. A sentence from one of his recent discussions of the problem is illuminating: "An occluded artery is no more an artery, but a plexus of sympathetic nerves in an abnormal condition.[7]" Although this point of view bears an intimate relationship to the point of view now being considered, it cannot well be included in this thesis without undue confusion.

The question arises as to the difference between excision and ligation with division of the artery as ordinarily practiced. It might be thought that ligation with division would satisfactorily block vasomotor

7. Leriche, R., and Stricker, P.: Observations on Juvenile Obliterating Arteritis, Brit. J. Surg. **16**:496 (Jan.) 1929.

impulses in the adventitia. However, as has already been noted, the effect of perivascular sympathectomy cannot be explained on the basis of nerve block. Apparently, whatever the explanation may be, there must be removal of a considerable number of fibers, some break, perhaps, in a complicated series of reflex arcs. Furthermore, the effects I am about to illustrate, so far as I am aware, have not been observed without excision as well as division.

The operation of arteriectomy should be considered on the aforementioned grounds in any case of complete arterial occlusion in an extremity, whether from disease, from trauma or from surgical ligation in the treatment for disease or trauma. One must except those cases of embolism in which embolectomy can be practiced within twenty-four hours. In my own experience, it has been employed associated with ligation for accidental trauma, in the treatment for arterial thrombosis, thrombo-angiitis obliterans and for false aneurysm. It has not been completely successful in averting gangrene, nor has the physiologic reaction of distal hyperemia been uniformly observed. In enough instances, however, definite hyperemia has resulted, even though there has been a previous ischemia, to suggest a sound theoretical basis for the operation. It is to be remembered, as will be emphasized later, that in most instances it is harmless.

REPORT OF CASES

In considering my cases, I shall group them into the four divisions already named, with discussion of each group as a separate problem.

Group I.—Ligation for Trauma.—CASE 1.—The record of this case, unfortunately, is not available. In 1923, Bardon and Mathey-Cornat[8] reported striking results in the rapid healing of chronic ulcers of the leg following periarterial sympathectomy. I had at that time an aged patient in the ward of the St. Louis City Hospital suffering from enormous dirty sluggish ulcers on the lower part of both legs, for which double amputation had been suggested. I attempted a periarterial sympathectomy on the femoral artery of the side presenting the largest ulcer. The artery was almost completely calcified, and during the manipulation it ruptured. Ligation was necessitated. In the course of this procedure the ligatures cut through several times, so that finally a considerable segment of the artery was destroyed and excised. This was, of course, a proceeding forced by accident without purpose at the time. Striking improvement in the ulcer on the side of the operation with the establishment of active granulation tissue and the beginning advance of epithelium was observed before the patient left the hospital about ten days later, against advice. There was never any disturbing coolness of the foot. That this result should have occurred in any patient with advanced arteriosclerosis after destruction of the main blood supply to the leg, was interesting. The only probable explanation is the performance of sympathectomy in the process of excision of the damaged arterial segment.

8. Bardon and Mathey-Cornat: Periarterial Sympathectomy in Chronic Ulcers of the Leg, Lyons chir. **20**:694, 1923.

This case is not presented as suggesting arterial excision for chronic ulcer or for arteriosclerotic ischemia. It is presented as an example of a traumatic division of a major vessel in which arterial excision was performed, albeit without purpose, and in which there was clinical evidence of improved circulation below the level of occlusion.

CASE 2.—A white man, aged 26, was shot through the upper part of the left thigh. The bullet injured the femoral artery and the vein just below Scarpa's triangle. There were coolness of the left foot and absence of palpable pulsations in the vessels. At a first operation by another surgeon shortly after the shooting, the exposure of the actual injury was frustrated by extremely active bleeding and a marked state of shock. The patient had lost considerable blood before admission. It was necessary to control the bleeding by packing the wound tightly.

During the course of the next twenty-four hours, his thigh became enormously swollen, and marked cyanosis developed in the lower part of the leg, which remained warm. The foot was pale and cool. The cyanosis was of an intense purple tinge, resembling that seen in traumatic cyanosis of the head and neck following crushing of the chest. The superficial veins were filled with blood. It was felt that perhaps the tight packing by pressure on the veins might account for a part of these phenomena. Apparently, at least, some blood was reaching the lower third of the lower part of the leg.

Following transfusion, twenty hours after injury, I reopened the wound and found the femoral artery and vein torn. Thrombosis had occurred, and the artery was not pulsating below the point of injury. Over an inch of the femoral artery and a corresponding amount of the damaged vein were excised. Large incisions in the fascia lata were made to relieve tension.

Following the operation there was no improvement in the patient's general condition, and he died five days later in uremic coma. There was no infection of the wound. Postmortem examination was not permitted.

There were changes in the local condition that may or may not have had significance. The day after the excision of the artery, there was a definite improvement in the area and degree of cyanosis of the lower part of the leg. The area was decreased in size by at least one-third, but the decrease was at the lower margin. The cyanosis was somewhat lighter in color. Warmth continued. The foot remained ischemic and before death early gangrene was established there.

It is impossible to ascribe these results to the arterial excision. Indeed, it is impossible to interpret the appearances with any clarity. The effect of the tremendous tension in the thigh from hemorrhage and packing cannot be overlooked. The case is presented as an example of a type of injury in which ligation is obligatory, in which excision is harmless, and in which this procedure may be done only with the hope that favorable results may be obtained.

Group II.—Arterial Thrombosis.—CASE 3.—A white, married woman, aged 38, with rheumatic heart disease accompanied by mitral stenosis and auricular fibrillation, had had an embolism of the right popliteal artery about five days before entrance. The embolus had supposedly originated in an auricular thrombus. The history suggested a rider embolus at the aortic bifurcation slipping later into the right vessel. She had had a possible cerebral embolism five months previously.

On admission, there was found coolness of the right leg from the knee down, without palpable pulsation in dorsalis pedis or posterior tibial arteries. There was a bluish, mottled discoloration of the right heel and of the plantar surface of the right metatarsal region.

For two days there was little change in the local condition. During the third day there was rapid advance in the signs of ischemia. Change of color was evident over the lower part of the leg, and the calf was indurated and swollen. Pain was excessive. The common femoral artery, previously palpable in the groin, could not be felt. The external iliac was palpable.

It was felt that thrombosis was extending rapidly up the vessel. With the patient under scopolamine-morphine supplemented by infiltration anesthesia, the common femoral was exposed at Poupart's ligament. The pulsation of the external iliac was traced down to this point. Here the vessel was ligated, and the entire common femoral artery, which was completely thrombosed, was excised (figs. 2 and 3). The excision included the first 5 mm. of both the femoral artery and the deep femoral artery. The latter bled, demonstrating some collateral circulation. This excision was done as a deliberate attempt to influence the collateral flow by sympathectomy.

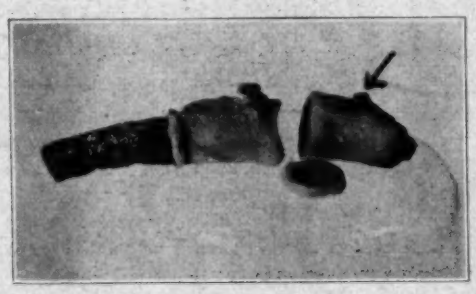

Fig. 2.—Gross specimen of common femoral artery removed in case 3. An oblique view of the cross-section is shown in figure 3. The arterial wall has contracted to little more than one-half its original length, baring a large part of the thrombus. The arrow points to the stump of the deep femoral artery. The obliteration of the vessel by thrombus is complete.

There was undoubted improvement of the circulation of the lower part of the leg following this operation. The discoloration in the upper portion of the discolored zone in the lower part of the leg disappeared and was replaced by a normal color. This area also showed recovery of warmth for the first time since admission to the hospital five days before.

The distal half of the lower part of the leg did not show improvement. A line of demarcation developed at about the middle of the lower part of the leg, well below the upper limit of the area where gangrene had earlier impended. Although it would have been interesting to have observed further changes, pain and toxemia became so extreme that supracondylar amputation was obligatory on the succeeding day. This was accomplished without incident under spinal anesthesia.

Convalescence proceeded uneventfully for a week, except for slight necrosis of the stump. On the seventh day the patient suffered from embolism of a cerebral vessel and of the left popliteal artery and promptly succumbed. Autopsy was not obtained.

Although gangrene was not averted and the outcome was amputation, the immediate improvement following arteriectomy was striking. The operation made no change in the mechanical conditions of the circulation; the artery was completely blocked before operation, and the vein was not disturbed. The probable explanation for the definite increase in warmth and improvement in color of a part of the extremity must be sought in the effect on the circulation of the incidental sympathectomy.

Fig. 3.—Cross-section of vessel shown in figure 2. Differential shrinkage has occurred so that the thrombus does not appear to block the lumen completely. Examination of the gross specimen reveals this as an artefact.

Goup III.—Thrombo-Angiitis Obliterans.—CASE 4.—A white man, aged 54, came to the hospital in October, 1927, suffering from typical thrombo-angiitis obliterans of four years' duration, worse in the right leg. Although claudication had been present, rest pain of an excruciating degree was the predominant symptom. During the first days of observation, a migratory phlebitis was present. No vessels were felt in either foot. The patient was treated by the internists with irradiation of the lumbosacral area. Two months later he returned with practically no change in symptoms, but presenting a superficial ulcer of the right heel. In

addition, he suffered from chronic myocarditis with auricular fibrillation and impending decompensation.

It was decided to try the procedure described by Lewis and Reichert,[9] namely, the ligation of the femoral artery in Hunter's canal for the purpose of encouraging collateral circulation through the deep femoral. The improvement which Lewis has described in several cases he attributes to the mechanical effect of shunting the force of each pulse wave into the alternative channel. In his descriptions of the operation Lewis mentioned excision of a portion of the vessel as a part of the procedure, but did not emphasize this element. It is done to obtain material for microscopic study.

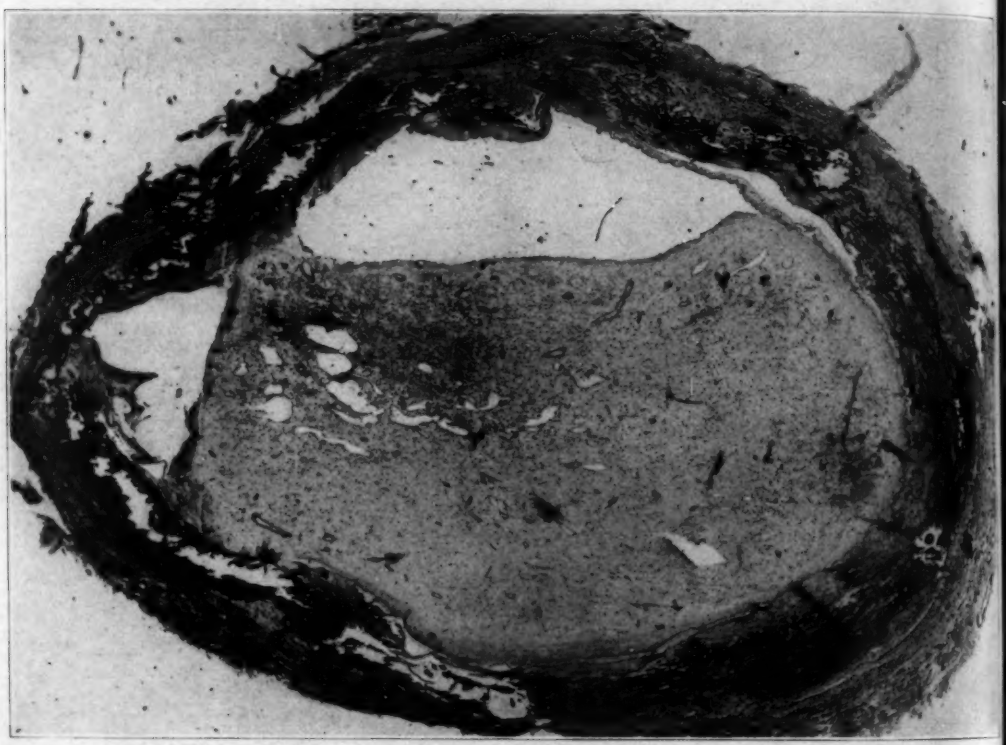

Fig. 4.—Cross-section of femoral artery removed in case 4. The characteristic changes of thrombo-angiitis obliterans are seen. In the gross, before fixation, the open channel shown was considerably smaller, being observed only as a thin slit between thrombus and vessel wall, which were actually in contact.

About 1½ inches (3.7 cc.) of both femoral artery and vein were therefore excised under local anesthesia. Both vessels were resected, because the tremendous perivascular inflammatory process prevented separation and identification of artery and vein. Microscopic study of the excised segments showed almost complete obliteration of the artery by an organized thrombus (fig. 4). The tissue changes were typical of thrombo-angiitis obliterans.

9. Lewis and Reichert: The Collateral Circulation in Thrombo-Angiitis Obliterans, J. A. M. A. **87**:302 (July 31) 1926.

The day following this operation, the patient reported a subjective feeling of warmth in the foot and leg. In his own words, it felt as if "the blood were trying to force through." The continuous pain was relieved and was replaced by a stabbing pain. There was a marked increase in the surface temperature of the foot. The return of color following obliteration of the capillaries by pressure was more rapid in this foot than in its mate. These changes were definite and lasted about four weeks. The ulcer bled freely during this time and diminished somewhat in size. Pain returned early and became a major factor in the care of the patient. The dorsalis pedis pulse was felt on one occasion.

After four weeks pain continued to increase, and the ulcer began to spread. Amputation above the knee became necessary, and an uneventful convalescence followed.

The obliteration of the lumen of the artery was so nearly complete that the mechanical effect of blocking the small amount of blood that could find its way through the remaining channel of the femoral artery must have been inappreciable. The pressure in the deep femoral artery probably was not elevated to a significant degree. Furthermore, the hyperemic reaction was too prompt to postulate mechanical dilation of the collaterals as a cause. The conclusion is forced that the effect followed the incidental removal of sympathetic fibers in the coat of the artery.

CASE 5.—A Greek, aged 39, entered the hospital in June, 1929, with dry gangrene of the right foot. Begininng two years previously, he had had three amputations of the left foot and leg. The first was an excision of the fifth metatarsal and little toe for bone necrosis; the second was an amputation at the junction of the middle and upper thirds of the tibia for spreading gangrene; the third was a supracondylar amputation for unhealed stump. At this time a clinical and pathologic diagnosis was made of thrombo-angiitis obliterans. Nearly a year before the last admission, gangrene began in the remaining right foot and slowly spread until on entrance it involved practically the entire foot distal to the astragalus. Pain was not marked until shortly before entrance. The lower part of the leg was cool, cyanotic and edematous. The popliteal and distal pulses could not be felt. The common femoral was easily felt. The femoral pulse could be traced part way down the thigh with great difficulty, in spite of extreme atrophy of the musculature.

In this case amputation of the foot was obligatory, but it was exceedingly desirable to save the one remaining knee joint. It was certain that amputation could not be successfully performed below the knee in the existing state of circulation of the lower part of the leg. With the experience of the last case in mind, the Lewis procedure was performed in the hope that the circulation would improve sufficiently to permit the conservative amputation. On this occasion arteriectomy was done, not based on the mechanical conception, but with the express purpose of accomplishing sympathectomy. A portion of the fused artery and vein, about 2 inches (5 cm.) long, was excised. Shortly after operation, the patient noted a sensation of increased warmth in the leg. This was readily confirmed by palpation. The cyanosis disappeared, and the elevated surface temperature remained. There was no improvement in pain. The gangrenous area became moist on the day following arteriectomy.

The evidence of improved circulation seemed to justify an upper tibial amputation, although ultimate healing of the stump could not be predicted with any con-

fidence. An amputation at the lower border of the upper third of the tibia was performed six days after the arteriectomy. The wound showed moderate necrosis. About two weeks later it was necessary to perform supracondylar amputation for persistence of unbearable pain and failure of the wound to heal. The final amputation stump of the thigh healed without incident.

In this case also, examination of the excised artery showed the possibility of practically no mechanical effect. The lumen was completely filled with thrombus which under the microscope showed a few

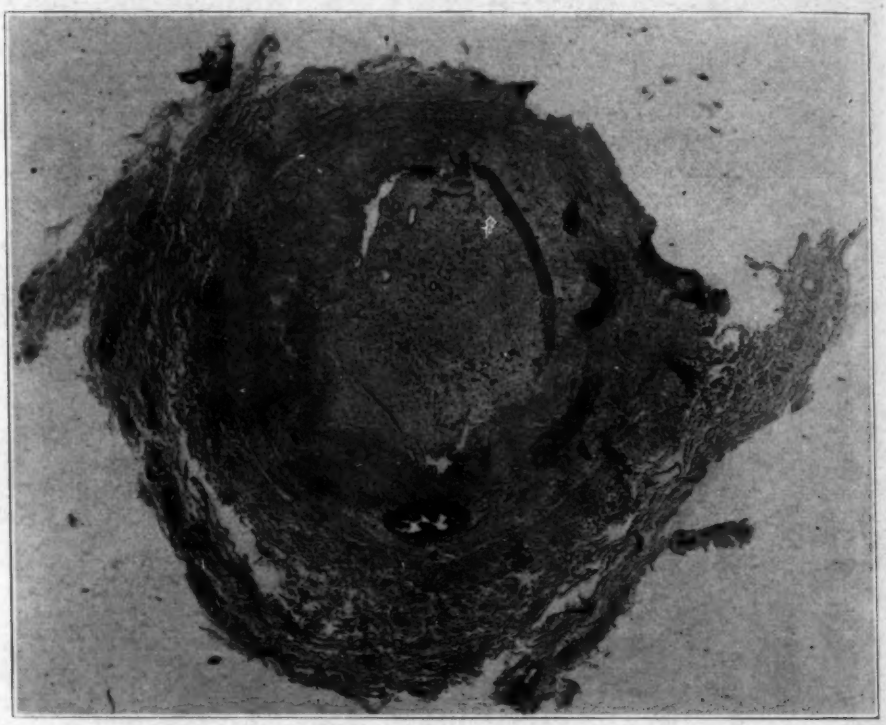

Fig. 5.—Cross-section of femoral artery removed in case 5. The characteristic changes of thrombo-angiitis obliterans are recognized. The complete blocking of the lumen by organized and slightly canalized thrombus is obvious.

minute channels (fig. 5). In this case also, the hyperemia was too prompt to permit a mechanical explanation of the improved distal circulation.

The unmistakable clinical evidence of improved circulation in these two cases following arteriectomy, even though amputation was avoided in neither, bears out Lewis' experience. I offer, however, a different interpretation of the results. It seems more probable that an incidental sympathectomy explains the phenomena. Both cases had practically

completely obliterated arteries; both cases showed immediate improvement in circulation following the excision of the vessels. In neither case could any significant alteration in proximal pressure have been accomplished by the blocking of the blood current.

Group IV.—Traumatic Aneurysm.—CASES 6, 7 and 8.—These three cases need not be described in detail, because in none of them is there any ground to affirm a favorable influence by arteriectomy. In each of them ligation above and below the sac of a false aneurysm was necessary on account of either extensive injury to the vessel or the density of scar tissue about the vessel. One was an acute traumatic aneurysm of the ulnar artery, one a traumatic aneurysm of the popliteal artery of long standing and one a similar aneurysm, even more chronic, of the femoral artery. In each case the segment of artery between the ligations was excised. In all three cases distal circulation was unimpaired after operation.

The point in mentioning these cases is to put on record another variety of vascular disease in which the proposed principle can be safely applied.

COMMENT

The cases in these four groups have in common the element of ligation of a major artery. In none of them could the ultimate usefulness of the vessel as a blood channel be hoped for. In none of them could the excision be harmful. In at least four, there appeared evidence of improvement in the distal circulation following the excision of a segment of the occluded artery.

The mechanical factors in the development of collateral circulation cannot be dismissed without recognition. The ligation of an accompanying vein as advocated on clinical grounds by Makins [10] and on experimental grounds by Brooks and Martin [11] must not be neglected. Furthermore, postural treatment, protection and heat must continue to be employed as useful agencies in ischemia. I do not propose that this operation replace tried measures.

The excision of an artery is not proposed when there is the possibility of danger. Danger of destroying collateral channels may exist in the excision of the walls of a true aneurysm and possibly of a false aneurysm as taught by Matas.[12] It is improbable that collateral channels existed in the badly scarred arterial walls of the two cases of chronic false aneurysm previously cited. In neither case was the sac

10. Makins, G.: Influence Exerted by the Military Experience of John Hunter, Lancet **1**:249, 1917 (The Hunterian Oration).

11. Brooks, B., and Martin, K. A.: Simultaneous Ligation of Vein and Artery, J. A. M. A. **80**:1678 (June 9) 1923.

12. Matas, R., in Keen: Surgery, Philadelphia, W. B. Saunders Company, 1909, vol. 5, p. 269.

itself excised. If there is any doubt as to the usefulness of the artery either as a main blood carrier or as the seat of collateral vessels, this procedure should be condemned.

The effect of the removal of the sympathetic supply to veins is an open question. In weighing the results of the operation described, judgment must be reserved as to the possible influence here.

One must not expect the removal of the perivascular sympathetics by arteriectomy to have a more permanent effect than results from removal by stripping. At the most, the effect may last from four to six weeks. In case 4 of the present series the time limit of the effect was well demonstrated. If by the operation sufficient hyperemia of the collaterals can be obtained to carry an extremity over the critical period of acute ischemia, much may be accomplished. In an occasional case this may mean ultimate salvation of the limb. Arteriectomy in cases of complete arterial occlusion is probably preferable to perivascular sympathectomy, because the removal of the fibers is more certain, more complete and much less difficult.

A further development of the idea of encouraging collateral circulation by operation on the sympathetic must be mentioned. If favorable effect can be shown by perivascular sympathectomy, it is logical to suggest that the more positive, permanent and rational operation of sympathetic ganglionectomy may have a place. If, for instance, one could diminish by lumbar sympathetic ganglionectomy the incidence of gangrene following acute division of the popliteal artery, a real addition would be made to one's resources. Experimental work now being carried on in my laboratory is directed toward the clarifying of this point.

There is a possibility that the ideas here expressed may help to clear up certain confused issues relating to this subject. If in every published report of ligation of a major vessel a detailed description of the operation were included, the confusion might in part disappear. It becomes essential to know in every such instance whether the ligation is accompanied by division or by excision of the artery, or by neither. Let me make a plea, parenthetically, for such information.

In conclusion, I must emphasize that I have presented no indisputable evidence that arterial excision improves collateral circulation by sympathectomy. I have presented suggestive evidence with the reasoning based thereon.

I urge only that in any instance of arterial occlusion in which excision is possible and apparently harmless, it be done with the intent to observe the results. Thereby the knowledge of these obscure phenomena may be increased. I suggest that thereby good results also may come to the individual patient.

SPLENECTOMY IN GAUCHER'S DISEASE*

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The literature on Gaucher's disease, by reason of its comparative paucity, has been kept well abreast of the time. It seems unnecessary to record a review of it.

At the Mayo Clinic, in 530 cases in which splenectomy was performed during the period of seventeen years, 1913 to 1929, inclusive, Gaucher's disease was encountered four times. In this article I shall not enter into a discussion of the theories advanced as to the etiology and pathology of the disease. Records of cases are given in detail as far as possible. I have been particularly interested in the value of splenectomy in this group, and there would seem to be a well grounded impression that in patients who have reached maturity removal of the spleen has a definitely beneficial effect.

REPORT OF CASES

CASE 1.—A woman, aged 30, came for examination on Jan. 26, 1920. She had married at the age of 17, and was the mother of eight children, all living and well. Her menses were regular, and she had had no miscarriages. Her chief complaint was a floating left kidney, which had been discovered seven years previously. For two years she had noted ready exhaustion and some dyspnea on exertion. There had been no edema of the extremities, no abdominal pain or discomfort and no urinary symptoms.

General examination disclosed a large mass filling the left upper abdominal quadrant. It had a sharp median edge suggestive of a greatly enlarged spleen. The thorax was negative to general and roentgenologic examinations. Nothing significant was noted in roentgenograms of the urinary tract. Results of urinalysis and of the Wassermann reaction of the blood were negative. Renal function was satisfactory. Examination of the blood was made on January 27.

The concentration of hemoglobin (Dare) was 80 per cent; erythrocytes numbered 4,760,000 and leukocytes 4,600 in each cubic millimeter of blood. Results of a differential count of 200 leukocytes were as follows: polymorphonuclear neutrophils, 78.5 per cent; lymphocytes, 20.5 per cent, and eosinophils, 1 per cent. The bleeding time was two and a half minutes, and the coagulation time was four minutes. Fragility of erythrocytes was normal. A pyelogram of the left kidney disclosed some downward displacement and rotation of the renal pelvis, with acute angulation of the ureter at the ureteropelvic juncture. A tentative diagnosis of a large cyst in the upper pole of the left kidney or of an extrarenal tumor was made.

Exploration through an anterior abdominal incision was advised. Operation on February 25 revealed a splenic tumor surrounded by dense adhesions. It was

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* From the Division of Medicine, the Mayo Clinic.

removed with some difficulty and with slight loss of blood. The left kidney was found to be displaced below the spleen, was movable, but not sufficiently diseased to warrant removal. The gallbladder, stomach and appendix were normal. The weight of the spleen was 1,450 Gm. The pathologic diagnosis was Gaucher's disease (fig. 1).

The patient made an uneventful convalescence and was dismissed from the hospital on the twelfth postoperative day. Examination of the blood on March 16 disclosed a concentration of hemoglobin (Dare) of 61 per cent. Erythrocytes numbered 3,620,000 and leukocytes 7,800 in each cubic millimeter of blood. A differential count of 200 leukocytes gave the following result: polymorphonuclear neutrophils, 59 per cent; lymphocytes, 37 per cent; eosinophils, 1 per cent, and basophils, 3 per cent.

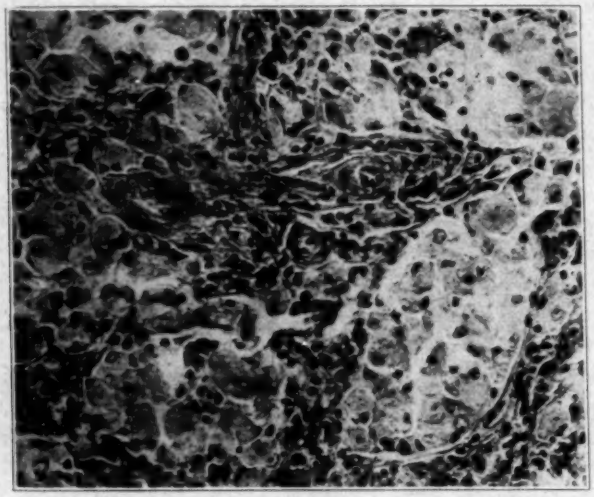

Fig. 1 (case 1).—Characteristic Gaucher's cells in spleen; × 250.

The patient's family physician, under date of Dec. 18, 1929, wrote: "She has been in the best of health since her operation. Has gained greatly in flesh, has been doing most of the work in a large family, and seemingly is good for a long life. I have confined her three times since her operation and she has done finely. These three children are healthy and strong, the last one being three months of age."

Case 2.—An unmarried woman, aged 36, came for examination on account of "female" trouble on May 15, 1923. She had two brothers and five sisters, all living and well. She had had pneumonia in infancy. Menstruation had begun when she was 13 years of age and had been regular until two years before she came to the clinic, when her periods had stopped abruptly. About the same time, during an attack of dengue, her physician had discovered that she had an abdominal tumor, which had been thought to be an ovarian cyst or uterine fibroma. She stated that there had been some enlargement of the liver as far back as she could remember. Jaundice had never been noticed, except during the attack of dengue. No history of abdominal pain or of loss of weight was elicited.

General examination revealed irregular enlargement of the abdomen. The sharp edge of a smooth liver could be felt reaching 17 cm. below the right costal margin, in the paramammary line. At this level, and occupying the central zone of the lower half of the abdomen, was a mass about 15 cm. in diameter, with an upper edge suggesting that of a greatly enlarged spleen. This mass could be palpated by vaginal examination in the anterior and left lateral culdesacs.

Nothing significant was found in the thorax, on either general or roentgenologic examination. Roentgenograms of the urinary tract gave negative results. In the urine, heavy traces of albumin, a few hyaline casts, and erythrocytes and pus cells in small numbers were found. Renal function and blood urea were within normal limits. The Wassermann reaction of the blood was negative. There were no pathologic changes in the eyegrounds. The blood picture was determined on

Fig. 2 (case 2).—Characteristic Gaucher's cells in spleen; × 250.

May 16. The concentration of hemoglobin was 80 per cent; the number of erythrocytes was 4,460,000, leukocytes 4,800, and platelets 112,000 in each cubic millimeter of blood. A differential count of 200 leukocytes disclosed the following: lymphocytes, 25.5 per cent; large mononuclears, 2 per cent; transitionals, 2 per cent; neutrophils, 69.5 per cent; eosinophils, 0.5 per cent, and basophils, 0.5 per cent. The coagulation time was eight minutes, and the bleeding time one and a half minutes. A diagnosis was made of a lower abdominal or pelvic tumor, associated with a greatly enlarged liver, and exploration was advised.

Operation was done on May 22, 1923. The lower abdominal tumor proved to be splenic; it lay in the pelvis by reason of a long pedicle. Removal was accomplished without difficulty or hemorrhage. The liver was enlarged, hard and friable. The uterus was atrophic. The pathologic diagnosis was Gaucher's disease. The spleen weighed 2,800 Gm. (fig. 2).

The patient made an uneventful convalescence and was dismissed from the hospital on the sixteenth day following operation. Under date of August 15, 1925, she wrote: "My color is good, and my general health has been excellent. Have been gaining weight rapidly. My liver is still very large. Have not had to consult a physician since my operation, more than two years ago." The last report

concerning the patient was from a friend, who stated that she had died very suddenly on May 24, 1929. The cause of death was given as cerebral hemorrhage.

CASE 3.—A woman, aged 26, of Jewish extraction,[7] who had no brothers or sisters, presented herself for examination on Sept. 7, 1927. She had married at 19 years of age, but never had been pregnant. She had scarlet fever in childhood. Menstruation had begun at the age of 13 years and had been somewhat irregular but without excessive flow. When she was 7 years of age her family physician had discovered, in a routine examination, that her spleen was enlarged. In spite of fairly marked anemia she had taken part in the ordinary pleasures and outdoor sports of youth. She always had been more easily exhausted than her companions. At the age of 9 years, she had been seen by a leading internist, who had made a diagnosis of Banti's disease, and he had advised splenectomy. Owing to the high risk given, surgical treatment had not been accepted, but several treatments with roentgen rays applied over the enlarged spleen had been tried. One year before she came to the clinic she had undergone tonsillectomy, and the operation had been followed by local hemorrhages. A month before she was seen at the clinic, she had a tooth extracted, and profuse gingival bleeding had persisted for two days. For the year prior to her registration at the clinic the patient had noticed rapid enlargement of the already large spleen. Sufficient food could not be taken at a meal without much distress afterward.

On examination, the patient was found to be somewhat anemic and in a fair state of nutrition. Pingueculae on the nasal side of each cornea were noted. The thorax was normal except for diminished breath sounds. The abdomen was greatly enlarged by a splenic mass which extended into the pelvis. The liver was moderately enlarged. No superficial lymph nodes of significant size were found.

Traces of albumin were found in the urine. The Wassermann reaction of the blood was negative. A roentgenogram of the thorax disclosed localized evidence of bronchiectasis in the lower lobe of the right lung. Complete examination of the blood was made on September 7. The concentration of hemoglobin was 51 per cent. Erythrocytes numbered 3,570,000, leukocytes 5,200, and platelets 86,000 in each cubic millimeter of blood. A differential count of 200 leukocytes disclosed the following: lymphocytes, 20 per cent; large mononuclears, 2 per cent; transitionals, 0.5 per cent; neutrophils, 76.5 per cent; eosinophils, 1 per cent, and reticulocytes, 3.5 per cent. The coagulation time was eleven and a half minutes (Lee method), and the bleeding time five minutes. Prothrombin time was prolonged in all tubes. Fragility of erythrocytes was normal. A dye retention test of hepatic function gave negative results. The concentration of serum bilirubin was 2.4 mg. per hundred cubic centimeters. The van den Bergh reaction was indirect. Gaucher's disease was the most probable diagnosis. A further trial or radiotherapy seemed more advisable than surgical treatment.

Following the treatment, the patient returned to the clinic, on October 17, for reconsideration of her condition. She felt much better and thought there had been some decrease in the splenomegaly. On this date the concentration of hemoglobin (Dare) was 49 per cent. Erythrocytes numbered 2,890,000 and leukocytes, 2,300. The bleeding time was twenty-two and a half minutes. The high risk of splenectomy did not seem to be warranted, and radiotherapy was again advised. At reexamination on November 28, the patient still maintained that her spleen had become smaller. The liver was not so large as in September. On November

7. In the cases in which the patients were of Hebrew extraction the fact is noted because formerly it was believed that this disease was peculiar to Jews. This belief has not been sustained.

28, the concentration of hemoglobin (Dare) was 46 per cent. Erythrocytes numbered 3,303,000, leukocytes 2,900 and platelets 76,000 in each cubic millimeter of blood. Coagulation time was eleven minutes (Lee), and calcium time, fourteen minutes; prothrombin time was prolonged in all tubes, and bleeding time was five and a half minutes. Retractility of the blood clot was marked in one hour and complete in three hours. The status of the patient made a decision as to future treatment somewhat of a dilemma, but operation finally was decided on.

Operation was performed on December 1. A huge spleen, projecting down into the pelvis, was found and was removed without great difficulty. The liver was large and there were tiny, shotlike nodules over it. A small piece of the right lobe was excised for examination. The gallbladder was distended, but no stones were felt in it. The spleen weighed 3,240 Gm.; the spleen and a specimen of liver showed changes characteristic of Gaucher's disease (fig. 3).

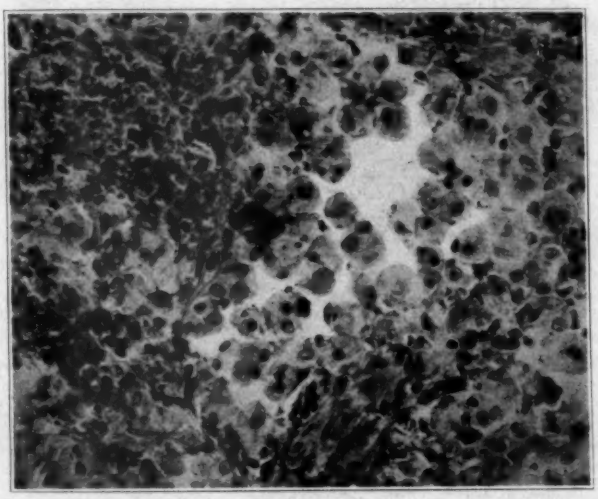

Fig. 3 (case 3).—Characteristic Gaucher's cells in spleen; × 250.

Convalescence was uneventful and the patient was dismissed from the hospital on the fourteenth postoperative day. During her stay in the hospital repeated tests of bleeding time were made and each showed it to be prolonged, ranging from twenty to fifteen minutes. At the same time, her blood platelets were rapidly increasing, from 264,000 on the twelfth day following operation to 480,000 on the fifteenth day. There were no hemorrhages at any time following splenectomy. The patient remained well and was not seen again until July 6, 1929. During the previous winter she had had pains in the right thigh and leg that had responded to treatment by heat and salicylates. She had gained from 10 to 12 pounds (4.5 to 5.4 Kg.) in weight. Menstruation had ceased until January, 1929, when she had had a normal flow for five days, followed by amenorrhea to the time of this last visit to the clinic.

General examination at this time did not reveal palpable enlargement of the liver; there was no adenopathy and nothing significant in the pelvis. On July 6, 1929, the concentration of hemoglobin (Dare) was 65 per cent; erythrocytes numbered 4,190,000, leukocytes 16,000 and platelets 168,000 in each cubic millimeter of blood. The differential leukocyte count was normal.

It was during this visit that changes in the long bones associated with Gaucher's disease were discovered in the roentgenologic examination. Complete roentgenologic examination of the skeleton in July, 1929, revealed the thorax, spinal column, pelvis and skull to be negative for changes characteristic of Gaucher's disease. There was enlargement of the medulla and thinning of the cortex of the humerus (fig. 4), radius and the upper end of the femur (fig. 5) on both sides.

The lesions demonstrable were of uniform type. The most marked change, general decrease in density, might be compared with senile osteoporosis. The

Fig. 4 (case 3).—Right humerus; enlargement of the medulla and thinning of the cortex are evident.

cortex, although markedly thinned, did not contain any areas of destruction. Trabeculation of the medulla was not as fine as it normally is, and the trabeculae appeared to have been pushed apart by some process between them rather than by actual destruction by malignant cells. These changes were most marked in the shafts of the bones. The lower ends of the femurs were somewhat widened.

Considered from the standpoint of differential diagnosis, the picture was rather typical of the bony changes in Gaucher's disease. There was no definite, well circumscribed region of destruction of bone suggesting metastasis or multiple myeloma.

This patient's general condition has remained satisfactory over a period of more than two years following splenectomy. Her domestic and social duties are carried on with ease as compared with the preceding two years of abdominal distress, progressive fatigability and advancing anemia. With the hemorrhagic tendency which was clearly manifest, the surgical risk of splenectomy was high, but that operation as a mode of treatment was well chosen would seem to be established by the period of good health the patient has enjoyed since.

CASE 4.—A Jewish woman, aged 33, married and the mother of one child who was in good health, came to the clinic on Oct. 22, 1928, seeking relief for recurring infections in the nares, associated with headaches. She had typhoid fever when she was 5 years old. Mentrual irregularities had not occurred. There had been occasional bleeding from hemorrhoids.

Fig. 5 (case 3).—Widening of lower ends of femurs.

General examination revealed enlargement of the spleen; the organ extended to the median line of the abdomen and to the level of the umbilicus. Enlargement of the liver could not be detected. There were small corneal pingueculae. Bilateral vestibulitis was found on examination of the nose and throat. The tonsils were small and fibrous. A passed specimen of urine contained a large amount of albumin. The Wassermann reaction of the blood was negative. Roentgenologic study of the thorax and long bones gave negative results. A concentration of hemoglobin (Dare) was 65 per cent. Erythrocytes numbered 4,140,000 and leukocytes 12,100 in each cubic millimeter of blood. A differential count of 200 leukocytes disclosed the following: lymphocytes, 13 per cent; large mononuclears, 2.5 per cent; transitionals, 2.5 per cent, and neutrophils, 82 per cent. A diagnosis of "possible Gaucher's splenomegaly" was made and splenectomy was advised.

Operation was postponed by the patient until June 5, 1929. At this time it was found that there had been some increase in the size of the spleen. There had been no new symptoms of note. A spleen weighing 1,000 Gm. and an accessory spleen of 125 Gm. were removed. The liver appeared normal. Stones could not be felt in the gallbladder. Pathologically, there were changes characteristic of Gaucher's disease in the spleen and in an accessory spleen (fig. 6).

Convalescence was uncomplicated. On the day following operation the leukocytes rose to 46,800; in a week they receded to 22,000. The number of blood platelets increased from 292,000, June 6, to 852,000 a week later. There were no appreciable changes in estimations of hemoglobin and erythrocytes. The patient was dismissed from the hospital on the fourteenth postoperative day. She was seen two months later in excellent condition. At that time, the concentration of hemoglobin was 70 per cent. Erythrocytes numbered 4,140,000 and leukocytes 13,000 in each cubic millimeter of blood. The differential count was normal. The urine contained only a slight trace of albumin.

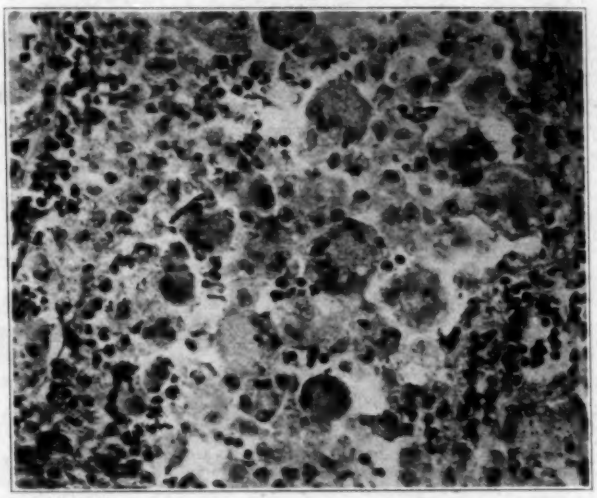

Fig. 6 (case 4).—Characteristic Gaucher's cells in spleen; × 250.

COMMENT

Four cases of Gaucher's disease, in which splenectomy was performed, are reported. All of the patients were women. The age at the time of operation ranged from 26 to 36 years. There was no history of familial tendency to the disease in any of the four patients. Two of the four patients are definitely known to belong to the Jewish race.

Gaucher's disease may not make any particular inroad into the general health of a patient. The unusual splenomegaly is the most frequent cause leading the patient to seek medical aid. Anemia was not present in cases 1, 2 or 4.

Three of the four patients have enjoyed periods of good health following splenectomy, ranging from seven months (case 4) to almost

ten years (case 1). Only one patient (case 2) has died. She lived for more than two years following splenectomy. The cause of death was cerebral hemorrhage.

Nothing significant has been discovered so far in the blood picture of Gaucher's disease to establish the diagnosis. Removal of a lymph node, splenic puncture, or trephining of the bone-marrow would seem to be warrantable means to employ in determining whether a case of obscure splenomegaly belongs to the group of Gaucher's disease. The roentgenographic changes in the bones may also be of great value in the final diagnosis. These changes are well shown in the roentgenograms taken in case 3. Hemorrhagic diathesis may be an outstanding feature of the disease, as illustrated in case 3.

Gaucher's disease in the female does not preclude the possibility of pregnancy, but that it may affect the menstrual life of the patient seems to be suggested. In the second patient, there was abrupt cessation of menstruation in the thirty-fourth year. The third patient has had a long period of amenorrhea since splenectomy, but the possibility that this may have been in part due to previous radiotherapy needs to be considered.

Splenectomy for Gaucher's disease, although not to be regarded as curative, must be looked on as a means of affording great relief to the patient, and possibly of arresting indefinitely the course of this obscure malady.

OCCURRENCE OF A TOXIC PROTEOSE FRACTION IN MATERIAL FROM VARIOUS SOURCES *

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A toxic proteose fraction has been isolated by Whipple and his co-workers [1] from the intestinal content obtained from patients with acute intestinal obstruction and from animals with obstruction experimentally produced. This observation has been confirmed by others, and the chemical nature of this fraction has been subjected to further investigation by Ingvaldsen and his co-workers.[2] Ellis [3] has been successful in isolating a toxic proteose fraction from the intestine of dogs dying from distemper, peritonitis and following operation on the adrenal gland and from animals dying from the administration of this material. The factors responsible for the production of this material and the rôle that it may play in various intoxications are unknown. It was thought that further information concerning its origin and significance might be obtained by investigating its occurrence in material from additional sources.

It is to be understood that the term, toxic proteose fraction, as used in this article refers to a certain fraction obtained by the methods of separation described by Whipple [1] and by Ellis [3] and does not imply that the toxic substances in this empiric fraction are necessarily proteoses in nature. We did not attempt to purify the fractions beyond the stages outlined by the foregoing investigators, because we wished to avoid loss and destruction of the material. Both methods of separation were found to be about equally efficient. For the identification of the fraction we have followed the symptoms, the changes in the blood and the gross pathologic processes induced in unanesthetized dogs by its intravenous administration.

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* Submitted for publication, March 18, 1930.

* From the Department of Physiology, State University of Iowa.

1. Whipple, G. H.; Rodenbaugh, F. H., and Kilgore, A. R.: Proteose Intoxication, J. Exper. Med. **23**:123, 1916.

2. Ingvaldsen, T.; Whipple, A. O.; Bauman, L., and Smith, B. C.: The Rôle of Anhydremia and the Nature of the Toxin in Intestinal Obstruction, J. Exper. Med. **39**:117, 1924.

3. Ellis, J. W.: Cause of Death in High Intestinal Obstruction, Ann. Surg. **75**:429, 1922.

EXPERIMENTAL WORK

Normal Intestine.—In order to evaluate properly our observations, it was necessary to know the degree of toxicity of normal intestine. The literature concerning this question is conflicting. Davis and Stone,[4] Whipple and his co-workers,[5] Ellis [3] and other investigators have regarded it as being practically nontoxic. Other workers have found it to have a variable degree of toxicity. Our investigation is limited to a study of the occurrence of the toxic proteose fraction and is not concerned with toxins of any other nature that may be present. The dogs were killed with chloroform or ether. The entire small intestine was removed, slit open and the mucosa and adherent content scraped away. The proteose fraction was prepared from this material in the usual way. The animals were selected from the stock used for experimental purposes and had been without food for the previous twenty-four hours. Nothing abnormal was noted about the animals, or the condition of their intestines.

When the material was prepared from the small intestine of a single average-sized animal, we invariably failed to obtain a fraction that would cause definite intoxication or death. However, when the fractions from four or more intestines were compounded and injected into a single animal, the effect was always severe intoxication or death. We can say from our experience that one intestine yielded approximately one fourth of a lethal dose of this fraction. The symptoms and pathologic changes were indistinguishable from those observed when the material was prepared from the content of an obstructed intestine. Fatal doses usually caused death in from six to eighteen hours. The symptoms and pathologic changes have been described in detail by others.[1] The animals might appear normal for a few minutes after injection and then show vomiting, salivation, prostration, retching, bloody diarrhea and coma. The blood showed a rise of nonprotein nitrogen, concentration of cells and sometimes a decrease of the chlorides. The necropsy showed splanchnic congestion and hemorrhages which were most prominent in the duodenum but which often extended throughout the entire intestine. Blood was present in the lumen of the intestine. Although our experiments were somewhat limited, we failed to find that autolysis of the fresh intestine with chloroform and toluene appreciably increased the yield of this material.

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4. Davis, D. M., and Stone, H. B.: Studies on the Development of Toxicity in Intestinal Secretion, J. Exper. Med. **26**:687, 1917.

5. Whipple, G. H.; Stone, H. B., and Bernheim, B. M.: A Study of a Toxic Substance Produced by the Mucosa of Closed Duodenal Loops, J. Exper. Med. **17**:307, 1913.

Obstructed Intestine.—We have been able to confirm the observations of previous investigators as to the occurrence of a toxic proteose fraction in the small intestine of dogs dying from obstruction experimentally produced or from an injection of the proteose fraction. In addition, we have been able to obtain it from the content of closed colon loops which were removed after a duration of two weeks. We were able to prepare a lethal dose from the small intestine of a man dying from Hodgkin's disease. The small intestine from a child, aged 16 months, dying from malnutrition and obstruction of the colon, failed to yield a potent fraction. This is the limit of our experience with human material.

Obstruction of the Portal Vein.—Ellis [3] reported the presence of the toxic proteose fraction in the intestine of dogs dying of a thrombosis of the portal vein. The duration of the condition was not reported by him. We have searched for this material in the intestines of dogs dying from a complete or partial occlusion of the portal vein, with the idea of determining how rapidly this material may appear in the intestinal tract in quantities sufficient to give symptoms. The intestine of one dog dying in two hours after complete portal obstruction yielded a lethal amount for a dog weighing 7 Kg. The material from a dog with a similar condition which died in one hour failed to yield a fraction of definite toxicity. The large mesenteric vein was ligated in a dog and caused death in four and a half hours. The fraction prepared from this animal's intestine caused only mild toxemia. The material from the intestine removed from a dog after a partial but effective occlusion of the portal vein of five hours' duration caused a definite but not fatal intoxication in a small dog. On the whole, these results seem to indicate that an interference with the blood supply to the intestine causes a greater quantity of the toxic fraction to appear in the intestine. However, the quantity was less than that found in the intestine from dogs dying in about the same time from injection of proteose. It is possible that the large amounts of bloody exudate into the intestines, as the result of portal ligation, may have lessened the quantity of material isolated.

Histamine Shock.—The fractions prepared from intestines of dogs which had received shock doses of histamine for several hours did not appear to be more toxic than the fractions prepared from normal intestine.

Spleen.—We failed to isolate a fraction of appreciable toxicity from 20 Gm. of spleen allowed to autolyze in phosphate buffer for ninety hours. However, when aliquot portions were inoculated with the contents from the lower part of the ileum and anaerobically incubated for ninety hours, they yielded a lethal dose of this fraction.

Liver.—We have been able to obtain a lethal dose of this fraction from the liver of dogs in some instances. In other cases only a slight reaction was noted. We are unable to account for these apparent inconsistencies.

Tissue Autolysis and Anaerobic Putrefaction.—When muscle, intestinal mucosa or spleen in quantities of from 10 to 40 Gm. were allowed to undergo autolysis in a buffered phosphate solution for periods of from twenty-four to ninety hours at 38 C., we were unable to demonstrate the presence of appreciable amounts of this toxic fraction. However, when aliquot portions of these substances were inoculated with the contents of the lower part of the ileum and incubated anaerobically as stated, we were invariably able to isolate a fraction which caused severe intoxication and death of the animals that were given injections. The symptoms, changes in the blood and pathologic processes were indistinguishable from those noted in animals that were given injections with material obtained from an obstructed intestine.

COMMENT

Our experiments show that a toxic proteose fraction could be isolated from material from various sources. The quantity of material obtained from each source was too limited to permit a detailed study of its chemical and physical properties. The effects produced by the injection of this material were the same regardless of its source. The symptoms and pathologic changes were for the most part typical of those noted in the animals dying from acute intestinal obstruction. The most noteworthy exception was the behavior of the blood chlorides. The whole blood and plasma chlorides were usually somewhat lowered. However, some animals in a condition of severe intoxication showed no change in blood chloride concentration. The latter is in harmony with the observations of Haden and Orr [6] that proteose fractions prepared from the content of obstructed intestine may cause little change in blood chlorides.

We believe that the failure of other investigators to obtain a toxic proteose fraction from normal intestine and other sources was due to the fact that they worked with too small a quantity of material. Thus the material obtained from the small intestine of one normal animal may cause such a mild reaction that it might be regarded as nontoxic, while the compounding of three or four such portions may represent a lethal dose. The absence of any easily detectable biologic reaction other than the determination of the lethal dose for dogs make progress in this direction slow and difficult. It is also to be recognized that the isolation of

6. Haden, R. L., and Orr, T. G.: The Blood Chlorides in Proteose Intoxication, J. Exper. Med. **48**:639, 1928.

this material is by no means quantitative. The possibilities of a loss of material due to destruction and adsorption by inert material are great.

Our experiments are not conclusive as to whether the proteose fraction is bacterial or nonbacterial in origin. The fact that bacteria or their products may have been present in all the material from which we isolated the toxic fraction, and that it was possible to increase greatly the yield of this material by anaerobic autolysis in the presense of the intestinal flora may be interpreted as indicating a bacterial origin. On the contrary, it is hard to explain its rapid accumulation in the intestine of animals after ligation of the portal vein or poisoning with a lethal dose on the basis of bacterial activity alone. It is well recognized that antiseptic autolysis in vitro may proceed differently from autolysis in vivo. Crucial evidence on this point might be obtained if sufficient quantities of sterile tissue were available. The observations of Towner [7] and of Ellis and Dragstedt [8] would indicate that it is difficult to obtain such tissues as pancreas and liver, completely sterile.

We believe our experiments indicate that the presence of a toxic proteose fraction in the intestine in various pathologic conditions should be regarded as merely an increase in the concentration of substances usually present in the intestine of healthy animals.

SUMMARY

A toxic proteose fraction has been isolated from normal intestine, obstructed small and large intestine, intestine of animals with obstruction of the portal vein and liver and from tissue allowed to undergo anaerobic autolysis in the presence of intestinal flora. The presence of this fraction was determined by the symptoms, changes in the blood and pathologic processes produced by its injection into dogs. It is suggested that the presence of this toxic material in various pathologic conditions should be regarded as indicating increased amounts of a material normally present rather than the elaboration of a new and specific substance.

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7. Towner, L. E.: The Pathogenic Physiology of Experimental Gangrenous Pancreatitis, J. A. M. A. **86**:1112 (April 10) 1926.

8. Ellis, J. C., and Dragstedt, L. R.: Effect of Liver Autolysis in Vivo: Preliminary Report, Proc. Soc. Exper. Biol. & Med. **26**:304, 1929.

A REVIEW OF UROLOGIC SURGERY*

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KIDNEY

Stone.—To the various types of urinary calculi usually described in the literature Braasch [1] added another form of lithiasis which is not generally recognized, and which from its nature may be termed "hysterical lithiasis." This unusual demonstration of an abnormal psychologic process is manifested by symptoms simulating those of acute renal colic. In order to make the deception complete, a stone will be produced by the patient shortly after the colic, which on casual observation may be mistaken for renal calculus. Nine cases of this unusual form of hysteria have been recorded at the Mayo Clinic; eight of these patients were women. All gave a history of having passed urinary calculi repeatedly; one patient claimed to have passed more than 200 stones. Examination of the specimens invariably showed the presence of inorganic material, which made the diagnosis of foreign body certain. Three of the patients were morphine addicts. Sympathy and attention obtained through invalidism were evidently major factors in the other cases. One patient secured prescriptions for alcohol in this manner. All of these patients denied inserting the stones, but when confronted with the chemical analysis, all but one patient admitted the accusation.

Another unusual type of urinary stone mentioned is that which occasionally is observed as causing hematuria. Gross calculi are not found on surgical exploration of the kidney. Microscopic examination

* Submitted for publication, Aug. 14, 1930.

1. Braasch, W. F.: Unusual Types of Urinary Lithiasis, J. Urol. **23**:1 (Jan.) 1930.

of the kidney will disclose the presence of numerous minute calculi in the renal tubules, which are moderately dilated. Such calculi may occur secondary to obstruction from blood clots accompanying an essential type of hematuria, although it would seem more probable that the calculi were an etiologic factor of the hematuria.

Hunt,[2] in considering some of the problems arising in the treatment for lithiasis, renal tuberculosis and neoplastic disease, stated that lithiasis is the most common surgical lesion in the kidney. During recent years at the Mayo Clinic, approximately 50 per cent of the operations performed on the kidney have been for calculus. The renal cause of lithiasis has not as yet been determined. The hypothesis that remote foci of infection are instrumental in the development of lithiasis has received much support. Other evidence tends to indicate that chemical changes incident to the advent of bacterial invasion of the kidney and urine may be instrumental in the precipitation and agglutination of the normal constituents of urine. Stones in the kidney are multiple in more than 40 per cent of the cases and are bilateral in approximately 10 per cent. At times stones in the kidney are associated with calculi in one or both ureters, which complicate the determination of proper methods of treatment. The significance of the complications of infection, urinary obstruction and destruction of renal function is emphasized by the frequency with which nephrectomy is necessary in treating renal lithiasis, an incidence so high as to reflect unfavorably on conservative nonoperative methods. At the Mayo Clinic, in a recent review of 941 cases in which operation was performed for renal calculus, nephrectomy was necessary in 334 cases (35 per cent) owing to infection and destruction of renal tissue. If a renal stone has not produced subjective symptoms and is less than about 0.5 cm. in diameter, its removal is not especially urgent. It should be given an opportunity to pass spontaneously. If, after observation for a certain period, the position does not change but the size increases, early removal should be considered. Repeated renal colic from a calculus of considerable size retaining its position in the kidney is sufficient indication for removal. Another exception to the rule that renal calculi should be removed surgically when the diagnosis is established is when the condition occurs in aged patients without apparent symptoms and without diminution in renal function. If branched stones are causing symptoms and injury to the kidney, the choice of conservative removal or nephrectomy is not always easy to determine. In the presence of adequate renal function conservative removal of the stone is the method of choice. Nephrectomy is easier in cases of large branched stones, but conservation of renal tissue under such difficulties is possible in the hands of a skilled surgeon.

2. Hunt, V. C.: Problems Related to Surgical Lesions of the Kidney, Ann. Surg. **91**:92 (Jan.) 1930.

In cases of ureteral lithiasis associated with renal stone, it is not always possible to determine the amount of infection and of renal function previous to removal of the ureteral calculus, particularly if the ureter will not permit the passage of a catheter. It may be best to remove the ureteral calculus first, if it is situated in the lower half of the ureter, and to determine the renal function and degree of infection later. If a ureteral stone is situated in the upper half of the ureter, it may be removed simultaneously with the calculus from the kidney through a posterior incision, if a conservative operation can be accomplished, or simultaneously with nephrectomy, if the radical operation is indicated. In case of the latter procedure, nephro-ureterectomy to below the ureteral stone has proved the method of choice.

Bilaterality of renal lithiasis is serious in proportion to the amount of renal injury and infection. It has seemed best to operate first on the side to which acute symptoms have been referable. In the absence of acute symptoms but with difference in function of the two kidneys, operation on the kidney with the better function is preferable.

Hunt has found it possible to remove stones by pelviolithotomy in 85 per cent of cases. This operation has been reserved for cases in which the stones are inaccessible through the pelvis because they are encysted in the terminal calices and situated rather superficially under the renal capsule. In the series of 941 cases of lithiasis there were 15 deaths, a mortality of 1.6 per cent. The mortality rate in 607 cases in which conservative operations were performed was 1.3 per cent as opposed to 2.1 per cent in cases in which nephrectomy was performed.

The upper part of the urinary tract seldom is alone the site of tuberculosis, and primary tuberculosis of the urinary tract rarely, if ever occúrs. It is generally accepted that tuberculosis of any part of the genito-urinary tract is hematogenous in origin. To determine the incidence of bilaterality of renal tuberculosis at the Mayo Clinic, a review was made of the operative and nonoperative cases during a ten year period. During this time nephrectomy was done on 574 patients, and 264 patients were observed on whom operation was not performed. In the latter group the diagnosis of renal tuberculosis was definitely established and all of the cases were considered nonsurgical, with the exception of 43 patients who refused nephrectomy. Approximately 73 per cent of the cases of renal tuberculosis were regarded as suitable for nephrectomy. The 221 cases were considered nonsurgical because of bilaterality in 77, occlusion and relative freedom from symptoms in 48, active and advanced pulmonary tuberculosis in 37 and extensive and advanced tuberculosis elsewhere in 38. In 10 cases in which nephrectomy had been performed for tuberculosis of one kidney, tuberculosis of the remaining kidney was found; in 4 nonoperative cases, bilateral renal tuberculosis was proved at necropsy. The diag-

nosis of bilaterality in the 77 cases was definitely established in most instances through the presence of bacilli of tuberculosis in the secretion from both kidneys or through inoculation of guinea-pigs. Definite evidence of bilateral renal tuberculosis existed in 91 of the nonoperative cases. Among those cases in which nephrectomy was performed, evidence of bilaterality existed in 20. There were 14 deaths (2.4 per cent) in the series of 574 cases in which nephrectomy was performed for renal tuberculosis; in the last 357 cases there were only 7 deaths (1.9 per cent). In general, there has been a mortality of 20 per cent within five years, with partial recovery of 80 per cent of the patients; 60 per cent have been completely cured, and 20 per cent have had persisting vesical symptoms. The shorter the duration of the disease and the less extensive the renal involvement and cystitis, the better will be the result. Braasch recently reviewed 65 cases in which nephrectomy was done between five and fifteen years ago and in which advanced secondary ulcerative cystitis was present with markedly reduced capacity of the bladder. Among these there was a five year mortality of 37 per cent. The condition of the bladders of 30 per cent of patients who were living was not improved. Early nephrectomy, before advanced involvement of the bladder occurs, insures more satisfactory results than may be expected in cases in which there is advanced involvement of the genito-urinary tract.

Most malignant lesions of the kidney tend to metastasize rapidly through local extension to perirenal structures and to the renal vein, which provides direct paths for remote metastasis. In the absence of demonstrable metastasis and fixation of the kidney by direct extension to surrounding structures, nephrectomy affords the best prognosis. The anterior transperitoneal route facilitates removal of large tumors entirely inaccessible through the usual posterior incision.

Hydronephrosis.—Stevens [3] presented a series of twenty-three cases in which surgical treatment was given for obstruction at the ureteropelvic juncture. In twenty of these cases the condition could probably have been corrected by operation with preservation of the kidney if a correct diagnosis had been made early. The most common obstruction at the ureteropelvic juncture is that caused by aberrant vessels going to the lower pole of the kidney. Some degree of ptosis of the kidney may be necessary before these vessels will interfere with the free flow of urine in the ureter. The anomalous vessels may be anterior to the surface of the kidney. In five of seven cases in which the condition was noted the vessels passed anterior to the ureter, and in two, posterior. In the series of twenty-three cases there were thirteen of hydro-

3. Stevens, A. R.: Hydronephrosis Due to Obstruction at the Uretero-Pelvic Junction, J. Urol. **23**:493 (May) 1930.

nephrosis due to aberrant vessels. Nephrectomy was done in ten. One patient had had symptoms for one week, another for two years, and the remainder of the patients from ten to twenty-three years. In all cases there was little if any function from the hydronephrotic kidney. In seven cases infection was proved to be present before operation. The kidneys in all of these cases were greatly enlarged, with thin and scanty parenchyma. In eight of the ten cases nephrectomy was performed on the left side. There was an equal number of men and women in the group, but in the latter the large kidney was always on the left side. There were four cases of obstruction from dense fibrous encapsulation of the ureteropelvic region. Careful search did not reveal any other factor. In three of the four cases, the corresponding kidneys were infected at the time of operation, and the peripelvic fibrous tissue was probably of inflammatory origin. Trauma accounted for the condition in the fourth case.

Von Lichtenberg [4] stated that treatment of such an important structure as the kidney should be directed toward its conservation. From his conception of conservative surgical intervention and his experience in treating what he called "urinary constipation," he concluded that in the treatment for this condition a conservative method may be used, having for its purpose the elimination of the symptoms and the maintenance or improvement of the remaining renal function. A conservative procedure is indicated especially in all cases in which the condition is bilateral, or in which the other kidney is also injured and the conservation procedure is not contraindicated by infection. A temporary fistula of the kidney assists essentially in the success of the operation. The kidney must be sufficiently exposed to give a clear picture in situ. This necessitates removal of the twelfth rib and occasionally of the eleventh rib. The palliative procedure disconnects the pathogenic lesion whereas the radical operation removes it.

[*Editorial Note.*—In the last decade great strides have been made toward conservative renal surgery. Partial resection of the kidney, plastic operation on the pelvis and ureters, the resection of obstructing anomalous vessels, etc., have made nephrectomy a far less frequent operative procedure.

In line with this conservative type of surgical intervention is the effort made by those who teach the doctrine of ureteral stricture as a cause of renal stasis and who advocate repeated ureteral dilatation as a means of establishing more satisfactory drainage of the tract. The rationale of the latter procedure is still *sub judice,* and the subject is of caustic controversy. Nevertheless, both ureteral dilatation and conservative operations on the kidney are procedures which illustrate

4. von Lichtenberg: Hydronephrosis, Am. J. Surg. **7**:747 (Dec.) 1929.

the definite trend toward making every effort to preserve functioning renal parenchyma whenever possible.]

Barringer [5] expressed the belief that there are two main reasons for conservatism in operating for hydronephrosis and hydropyonephrosis. First, present-day methods of examination are inadequate for determination of precisely what a kidney is doing. Second, it is not known how far a kidney is capable of returning to normal. An infected kidney can return to normal even if largely infected, but there is no standard by which it can be ascertained, prior to operation, what a kidney can do.

Walters [6] stated that a review of the literature on ureteropyelonephrostomy indicates that if the anastomosis is correctly made, function will be satisfactory. He reported two cases in which anastomosis was successful. In these two cases lateral anastomosis was made between the ureter and the dependent portion of the hydronephrotic renal pelvis. A ureteral catheter was placed temporarily through the anastomosis to serve as a scaffolding for healing. In the first case the catheter had been inserted in the ureter in order to decompress the renal pelvis and was there at the time of operation. It was carried into the pelvis through the anastomosis and maintained in place for twenty days, when it was removed. Temporary nephrostomy was done in this case to prevent tension at the point of anastomosis. A no. 14 French catheter was used, which was removed on the eighth day. In the second case, the cause of the obstruction was a dense scar of fibrous tissue at the ureteropelvic juncture. Connective tissue had extended to a point below this, angulating the ureter. When first exposed this angulation appeared to be the site of obstruction. After it was free, an opening was made in the ureter about 3 cm. distal to this point and a catheter was pushed toward the renal pelvis as a probe. It was then found that the obstruction had not been relieved but existed at the ureteropelvic juncture. When the ureter was dissected to this point the obstruction was found, and a lateral anastomosis was made between the ureter below and the pelvis above. A ureteral catheter was carried through the anastomosis and out of the incision through the ureterostomy opening in which it was left for thirteen days. A nephrostomy tube was also used and removed on the tenth day following operation.

Hirst [7] summarized present knowledge of the kidney in cases of pregnancy and presented certain additional information. The title is

5. Barringer, B. S.: Discussion of Hydronephrosis, Am. J. Surg. **7**:752 (Dec.) 1929.

6. Walters, Waltman: Ureteropyelonephrostomy for Urinary Obstruction at the Uretero Pelvic Junction, Ann. Surg. **91**:101 (Jan.) 1930.

7. Hirst, J. C.: The Kidney of Pregnancy, Am. J. Obst. & Gynec. **18**:528 (Oct.) 1929.

used in a broad sense to include: (1) the diagnosis of hydronephrosis, infected hydronephrosis and pyelitis complicating pregnancy, with the comparison of the relative frequency of appendicitis and disease of the gallbladder; (2) the relation of hydronephrosis and pyelitis to early and to late gestational toxemia; (3) differential tests of renal function and pyelograms to discover additional factors in the cause of the common hydronephrosis in pregnancy, with special attention to the possibility of ureteral edema or chronic passive congestion that might be a contributing cause of late gestational toxemia and eclampsia, and (4) an attempt to differentiate renal and hepatic toxemia of pregnancy by the effect of the administration of a blood pressure lowering preparation from liver.

From his review of important articles on the subject, and from his own experience, Hirst concluded: (1) cystoscopic urologic diagnosis is of significance in obstetric service, and, when carefully performed, no risk is involved; (2) vasodilatation and circulatory stasis of the distal ureter may directly or indirectly be concerned with late gestational toxemia; (3) early and late toxemia are essentially different, the latter being primarily renal in origin, and (4) the liver preparation appears to bear insufficient specific action to separate a hepatic type from the late forms of the toxemias of pregnancy.

From a summary of data concerning ninety-seven obstetric patients who were subjected to cystoscopic and pyelographic examinations, the following significant facts were obtained: Ureteral obstruction appeared only four times; the absence of frequent obstruction presupposes some additional factor responsible for impaired drainage not accounted for by atonic ureteral dilatation or latent infection so common in pregnancy. The impairment is believed to be circulatory in the form of intermittent vasodilatation or chronic passive congestion around the distal ureter, evidenced by edema of the orifice in the form of irregularity of shape and puffing. Jaundice did not appear in any case, but in one instance subacute exacerbation of a chronic cholecystitis followed ureteral catheterization. Even if the renohepatic interrelation is of significance in infection and toxemia, it appears that it is not particularly significant in a careful cystoscopic examination of the obstetric patient. Other harmful results of urologic investigation included troublesome increases in severity of chronic pyelitis in two patients, and in one patient it precipitated labor at term.

Pyonephrosis.—Paschkis [8] stated that epithelial changes in the urinary tract simulating cystitis cystica and glandularis are rare and their etiology is unknown. The inference is that there are stimuli of

8. Paschkis, Rudolf: Pyeonephrose mit Ureteritis cystica, Ztschr. f. urol. Chir. **28**:64, 1929.

various types which cause an otherwise normally functioning gland or cyst to develop to an advanced stage. In other cases such stimuli may cause epidermization of the mucous membrane. Paschkis observed cases of renal calculi in which the mucous membrane has presented a condition known as pyelitis glandularis.

The case of a woman, aged 55, who had right-sided colic with disturbances of the bladder, was reported. A history of hematuria and of trauma of the right side of the abdomen was obtained. Twenty-four years before, following a forceps delivery, a perinephritic abscess developed on the right side and was drained. Examination revealed closed right pyonephrosis. Intracapsular nephrectomy was performed. Pathologic examination of the kidney showed pyonephrosis. Chronic cystic proliferating ureteritis almost obliterating the lumen was found in the upper part of the ureter. Paschkis concluded that in childhood hydrohematonephrosis may have formed due to the injury; later, infection ensued causing both the pyonephrosis and the perinephritic abscess.

Lipomatosis.—Kutzmann [9] found that replacement lipomatosis of the kidney is of rare occurrence. He cited the case of a man, aged 56, who complained of continuous dull pain in the region of the right kidney, dysuria and frequency. A diagnosis of right calculous pyonephrosis was made. Intracapsular nephrectomy was performed. The kidney was found to be markedly adherent to all structures in the lumbar region, especially to the posterior peritoneum and diaphragm. The perirenal fat was fibrous and tough. These factors greatly hindered freeing the kidney from the adjacent structures and made the intracapsular procedure imperative. Nephrolithiasis, chronic diffuse nephritis, atrophy of the renal parenchyma and fatty degeneration of the renal hilus, which apparently had invaded the kidney, were found. Recovery was uneventful.

Twenty-eight proved cases and nine doubtful cases were noted in the literature. Kutzmann concluded that replacement lipomatosis of the kidney is always associated with severe infection of the kidney. Calculous disease was associated in 71 per cent of the cases. The sexes and the side involved were about equal; pathognomonic signs or clinical symptoms were not apparent. The cases reported earlier were found at necropsy, whereas those recently observed were found at operation. Treatment is directed to the associated condition and usually is nephrectomy. Such kidneys are painful, badly infected and functionless. The pathogenesis is hypothetic. The process of replacement is probably one of invasion of perirenal, peripelvic and hilus fat along the large vessels through the renal hilus.

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9. Kutzmann, A. A.: Replacement Lipomatosis of the Kidney, Proc. Ninth Meeting Clin. Soc. Genito-Urin. Surg., San Francisco, July, 1929.

[*Editorial Note.*—Replacement of renal parenchyma by fat is of rare occurrence, and has been considered only occasionally in the American literature. The European literature, however, contains many hypothetic considerations concerning its unknown etiology and pathogenesis.

The substitution of renal parenchyma by true adipose tissue has been variously designated in the literature as lipomatous nephritis, lipomatous paranephritis, lipoma diffusum renis, substitutio renis adiposa, lipomatosis renis, fatty transformation of the kidney, fat replacement of the kidney and fatty degeneration of the kidney. These terms are more descriptive of the latter stages of this pathologic anatomic process, in which the entire parenchyma of the kidney may have disappeared. In the earlier stages in which the changes have not as yet occurred in the hilus and polar regions of the kidney, the term "lipomatous paranephritis" has been considered more descriptive by certain observers. The process has not been satisfactorily explained. The condition is usually classified with the paranephritides. The fat either may surround the kidney or may limit itself to individual areas, usually at the hilus or polar regions of the kidney. It may even involve the ureter, assuming colossal dimensions. The fat substitution usually parallels an atrophying renal process.

The theories concerning the pathogenesis of this condition may be placed in two essential groups: a minority of authors considers the primary growth to be from the fatty capsule, while coincidentally the fat of the hilus forces its way into the kidney, leading secondarily to atrophy. There is no overwhelming evidence to support this view. The majority of authors holds that the substitution of fat is secondary and considers that the atrophying process is of primary importance. To support the latter view it has been pointed out that at times retroperitoneal lipomas assume huge proportions, surrounding and pressing the kidney on all sides and yet not causing destruction or atrophy of the parenchyma of the kidney. If the fatty growth were of a primary nature, histologic examination should reveal traces of renal tissue, which has never been the case. Between the fat tissue and the remaining atrophic parenchyma of the kidney there is usually a sharp boundary.

Calculous disease of the kidney seems an important factor. Analysis of thirty-five cases revealed calculous disease in twenty-six (79 per cent), bilateral cases of replacement lipomatosis, three cases, and bilateral renal and ureteral calculi, combined with an infection, two cases. Destruction of the pelvis and parenchyma of the kidney and finally the familiar picture of pyonephrosis result. The presence of calculi and the chronicity of the infection may result in a proliferative and invasive power to the already hyperplastic peripelvic fat about the renal hilus and in a renal invasion around the large vessels.]

Rupture.—Shapiro [10] stated that rupture of the kidney may result from direct trauma by which the kidney is driven against the lower ribs or against the transverse processes of the first and second lumbar vertebrae, from indirect trauma, from muscular action producing abrupt flexion, such as jumping backward or dodging objects, or it may occur spontaneously. The seriousness of rupture of the kidney depends mainly on the extent and site of the injury. A subcapsular rupture, after a few days of pain in the loin associated with hematuria, will entirely disappear. In this type of rupture there is a tearing of renal tissue, but the capsule remains intact. From the injured tissue there is an outpouring of blood and urine, with the result that the intracapsular volume increases and with it the intracapsular pressure rises also. A total rupture with severance of the main vessels will rapidly exsanguinate the patient, or, with a torn peritoneum, extravasation of urine into the peritoneal cavity will result in fatal peritonitis. The blood and urine escape through the torn capsule of the kidney into the retrorenal tissue between the kidney and the peritoneum, forming a mass of varying size and composed of a mixture of blood and urine.

A bleeding kidney is evidenced clinically not only by hematuria but by ecchymosis, or subcutaneous hemorrhage. The latter is usually found in the flank and may prove a valuable aid in diagnosis. The cardinal symptoms of ruptured kidney are pain of varying degrees, tumor and hemorrhage, together with the condition of shock. The pain is usually in the loin but may radiate down the thigh, to the penis and scrotum.

Secondary hemorrhage has sometimes followed rupture after the patient has apparently recovered from the injury. Other sequelae of rupture of the kidney are suppuration, calculi and cysts, and even nephritis and malignant neoplasms have been reported.

In any treatment for ruptured kidney attempts should be made to conserve the function of both kidneys. The majority of such injuries will heal by expectant treatment. Whether operation is necessary will be determined by the extent of bleeding. Surgical intervention is indicated when there is a gradual rise in the pulse rate and a sharp drop of the erythrocytes, the hemoglobin and the blood pressure. Conservative procedures of tamponade, suture or drainage should be carried out if the bleeding is such that a tampon will check it, if the kidney is only slightly injured or if the fragments can readily be approximated by suture. If the bleeding is uncontrollable, if the tear in the kidney cannot be sutured successfully, if the artery and vein are shorn off, if the pelvis is severely torn or if the ureter is entirely severed, nephrectomy is indicated. Removal of the kidney is also indicated if

10. Shapiro, E. Z.: Ruptured Kidney, J. Urol. **23**:343 (March) 1930.

the rupture is associated with severe infection or disease such as hydronephrosis and calculi. Laparotomy is urgent if there is suspicion of torn peritoneum or injury of the abdominal viscera.

Perirenal Tumors.—Crabtree [11] stated that perirenal lipomas and true fatty tumors of the urinary organs are to be distinguished from the lipomatous changes of chronic infections. Perirenal fatty tumors are more common than renal lipomas. They form two definite groups: one in which long-standing tumors by their size produce symptoms of pressure; the other, tumors in which the clinical picture is suggestive of malignancy. Pathologically, these fatty tumors range between normal fibrous fat and sarcoma. In the pure lipomas the blood supply to the tumor is meager and the fibrous capsule incloses the tumor in such a way that surgical enucleation of a large mass is not difficult. Lipoma of the perirenal and retroperitoneal area is more common in women. The disease seems independent of associated organs and occurs with equal frequency on either side. In some cases a history of injury is given. In other cases of long standing the tumor grows rapidly after injury or some form of irritation, such as inflammation of the appendix, or colitis or for no apparent reason.

The most common symptom is enlargement of the abdomen, often symmetrical. Since the fat is soft at body temperature the tumor is not definitely localized, a phenomenon which often leads to the diagnosis of ascites; this sometimes occurs even though the tumor is growing rapidly. The apparently normal fat content is not available for metabolism in these patients. In some of the cases studied loss of weight was rapid, although the tumor was not sufficiently large to produce derangements of physiology due to pressure.

The majority of cases reported have been diagnosed only at operation or at necropsy. Deformity of the kidney has not been recorded, but it has become displaced from pressure or its pelvic outline appears normal. Braasch's statement, that when the outline of the pelvis is normal it is not likely that the surrounding tumor is of renal origin, is confirmed in these cases. Whenever possible, operation is the treatment of choice. In cases of pure lipoma in which the lobulated masses are encapsulated, the mass, even though large, is often easily removed. These cases are usually not good surgical risks. Wahlendorf found an immediate mortality of 25 per cent in a series of 165 cases; other observers report a similar mortality rate. In many cases in which the patients survived operation, complete removal of the tumor had not been accomplished. Repeated operations were not well tolerated. Data are not available to determine longevity in those cases in which operation was incomplete or was not performed.

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11. Crabtree, E. G.: Perirenal Lipoma with Generalized Abdominal Lipomatosis, J. Urol. **23**:545 (May) 1930.

MacKenzie [12] reported a case of spontaneous perirenal hemorrhage occurring in a man suffering from polycythemia. Nephrectomy was performed, and the patient recovered.

Sixty-six cases of perirenal hematoma have been reported in the literature, but none has occurred in conjunction with polycythemia. Four have occurred in patients who had hemophilia. Spontaneous perirenal hemorrhage has been classified according to the source, such as primary, of unknown etiology, and secondary, due to some discoverable lesion.

BLADDER

Reflux,—Bronner and Schüller [13] stated that the vesico-ureteral or vesicorenal reflux is variously described in the literature as a vesicorenal backflow, forced ureters or gaping of the ureters. The lesion never occurs under normal conditions because of the valvelike action of the ureteral orifice. As soon as there is disturbance of the physiologic function of the bladder and ureters, the valvelike action of the ureteral orifice ceases and a vesico-ureteral or a vesicorenal reflux ensues. Conditions leading to disturbance in the action of the ureteral orifice are marked hypertonia of the musculature of the bladder due to tenesmus in different diseases, disturbances due to narcosis or lumbar anesthesia and ureteral rigidity in certain inflammatory conditions, leading to the so-called funnel-shaped orifice.

The case of a girl, aged 24 years, who had diffuse tuberculous cystitis and left renal tuberculosis in which a vesicorenal reflux developed on the opposite side, was reported. The first stage of the vesicorenal reflux of the right side was observed previous to operation, and it was thought that nephrectomy on the left side would cause the condition to disappear. To check up, cystograms made fourteen days, one month and one and a half months, and again fifteen months later, showed gradual progression of the vesicorenal reflux to complete hydronephrosis. The patient was observed during the entire course of the disease, and it was possible to study the various stages of vesicorenal reflux. First, there was only slight dilatation of the lower portion of the ureter with the urine entering this part of the ureter. Later the urine entered as high as the pelvis of the kidney and there was progressive dilatation of the entire ureter. In the third stage, tortuosity with occasional kinking of the ureter developed, leading to retention of the urine in the upper portion of the ureter and pelvis of the kidney. The final stage of the disease was marked by hydronephrosis.

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12. MacKenzie, D. W.: Perirenal Hematoma Primary with Polycythemia, J. Urol. **23**:535 (May) 1930.

13. Bronner, H., and Schüller, H.: Der Blasen-Nierenrückfluss (Vesikorenaler Reflux), Klinischen und röntgenologischen Beiträge, Fortschr. a. d. Geb. d. Röntgenstrahlen **40**:419 (Sept.) 1929.

The symptoms are in accordance with the various stages of the disease. First there is only a drawing sensation in the lower part of the back; then the sudden desire to urinate develops, especially noticeable on a change from the horizontal to the vertical position. It often develops into urinary incontinence. In the final stage, urination in two or several periods follows. The latter is due to the fact that during actual micturition the bladder expels the urine both into the urethra and toward the kidney.

Cystoscopy is the method of examination in vesicorenal reflux. The direct application of pyelography is contraindicated since the slightest pressure may lead to the opaque substance entering the venous system of the kidney. Among opaque mediums are a 12 per cent solution of sodium iodide or a 5 per cent solution of iodized oil.

The various diseases leading to vesicorenal reflux are: (1) Tuberculosis of the bladder and kidney. According to Bumpus, this is responsible for 40 per cent of all reflux and appears in 20 per cent of all cases of tuberculosis of the kidney; occasionally it may disappear spontaneously following removal of the diseased kidney or conservative treatment of the bladder. (2) Infections of the bladder or of the pelvis of the kidney. Reflux of this type is relatively benign and as a rule it disappears as the result of conservative treatment. (3) Conditions associated with retention of long standing, such as ureteral stricture and hypertrophy of the prostate. It has been noted by Bumpus that the vesicorenal reflux which accompanies enlarged prostate glands increases from 4.74 to 11.42 per cent following prostatectomy. (4) Implantation of the ureters into the colon as practiced in certain operations. Maydl's attempt to transplant the entire trigone of the bladder into the colon so as to prevent the reflux has not led to better results. From 70 to 80 per cent of all colonic transplantations of the ureters result in renal reflux, necessitating later the removal of the kidney. (5) Transvesical resection of enlargements of the lower portion of the ureter. (6) Certain instances of ureteral stones, producing partial obstruction. (7) Certain lesions of the spinal cord, and exceptional congenital lesions.

Whether or not vesicorenal reflux always leads to insufficiency of the affected kidney is not definitely determined.

Teposu [14] described two cases of vesicorenal reflux. The first case occurred in a man, aged 55, who, since 1916, had complained of symptoms referable to the bladder, and who in 1925 and 1926 had had three successive operations. A diagnosis of sclerosis of the trigone (due

14. Teposu, E.: Insuficienta orificiului ureteral si reflux vesico-renal, Cluj. med. **10**:579, 1929.

to scarifications from the operations) was made, and it was thought that this sclerosis was responsible for the vesicorenal reflux. Following the excision of the trigone, the lesion apparently healed. The second case was that of a girl, aged 14 years. The cause was not definite. The vesicorenal reflux was confined to the left side.

In connection with these two cases, Teposu considered the mechanism of vesicorenal reflux and arrived at the conclusion that it may be the result of the following three factors: (1) disturbance in the normal peristalsis of the ureter; (2) disturbances in the obliquity of the intramural portion of the ureter, and (3) insufficiency of the valvular function of the ureteral orifice.

The conditions that may lead to disturbance of the foregoing factors are acute or chronic inflammation, tuberculosis, lesions of the trigone, ureterocystoneostoma, prostatic hypertrophy, diseases of the nervous system (tabes dorsalis, poliomyelitis, multiple sclerosis) and spina bifida.

Tumors.—McCarthy [15] stated that in consideration of any technic in the treatment for new growths occurring in the bladder, diagnosis is the basic question. Precise diagnosis is necessary not only prior to operation, but by free mobilization at the time of operation. In cystoscopic transurethral and transvesical diathermy there should be a wider application with the largest possible electrodes. Results from radium and the application of deep roentgen rays have not been satisfactory, and their use is no longer advocated. Free mobilization of the bladder is advised as a preliminary step in cases in which open operation is performed. If all these measures fail, prompt cystectomy should be done.

Carcinoma.—Fey and Bompart [16] reviewed 108 cases from the literature of total cystectomy for carcinoma of the bladder. Bardenheuer performed the first operation of this type. The immediate results were not encouraging. Fifty-six (51.8 per cent) of the 108 patients died early. In all cases in which the ureter was placed in the urethra, and in 59 per cent of cases in which the ureter was transplanted to the intestine, the patients died. Transplantation into the vagina was followed by a mortality of 33 per cent. Cutaneous ureterostomy resulted in a mortality of 23 per cent. Eighty-five patients were operated on by a one-stage method; 50 (59 per cent) died. Twenty-three patients were operated on by the two-stage method; 6 (26 per cent) died. The late results of total cystectomy are not satisfactory.

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15. McCarthy, J. F.: A Consideration of Technique in the Management of New Growths of the Bladder, J. Urol. **23**:323 (March) 1930.

16. Fey, B., and Bompart, H.: A propos de la cystectomie totale pour cancer de la vessie, Paris méd. **2**:359 (Oct. 19) 1929.

The mortality is approximately 30 per cent for the first six months after operation, 40 per cent for the first year and 70 per cent for the first two years.

Fey and Bompart stated that cystectomy for carcinoma has received unjustified discredit at the present time. Carried out under certain conditions, such as early operation by the two-stage procedure and iliac ureterostomy, this operation would give results superior to those in use at the present time. The authors are of the opinion that this method will some day be the treatment of choice for carcinoma of the bladder.

Hernia.—Wakeley [17] stated that it is possible for the bladder to protrude through any of the hernial orifices, although the protrusion usually is inguinal or femoral. Inguinal hernia of the bladder is less common in women than in men, whereas femoral hernia of the bladder occurs almost solely in women. Of forty-two cases of the femoral variety, forty occurred in women. Hernia of the bladder may be classified as extraperitoneal, paraperitoneal and intraperitoneal, according to the relationship of the hernia to the peritoneum. In extraperitoneal hernia of the bladder the anterior or lateral extraperitoneal surface of the bladder enters the inguinal or crural canal. It is always small and rarely gives rise to symptoms. It takes the form of a direct inguinal hernia. In paraperitoneal hernia of the bladder the hernia may be direct or indirect; the bladder always lies on the inner side of the hernial sac. The serous covering of the superior surface of the bladder will form the inner wall of the peritoneal sac. It is the most common of the three varieties and the easiest to treat successfully. The bladder is usually situated at the inner and posterior part of the peritoneal sac. During operation, when the sac is dissected from the constituents of the spermatic cord, a definite increase in the thickness of the sac will be observed, and careful gauze dissection will demonstrate the adherent bladder. Intraperitoneal hernia of the bladder is a rare condition, but is more common than that of the extraperitoneal variety. In Wakeley's series of forty cases, it occurred in fourteen. These hernias usually are large, secondary in origin and practically always in the inguinal region. There is a complete hernial sac, and the upper and posterior part of the bladder enters the sac, which is external to the deep epigastric artery. Frequently the hernial sac contains, besides the bladder, loops of small and large intestine and omentum.

Any factor which increases the volume of the bladder favors hernia of the bladder; consequently stricture of the urethra and prostatic

17. Wakeley, C. P. G.: Hernia of the Bladder: Its Etiology and Treatment, Brit. J. Urol. **2**:1 (March) 1930.

enlargement are predisposing factors in old men, and a tight prepuce or a pinhole meatus may be considered predisposing factors in infants. Pregnancy is the most common predisposing factor in women. In the male the bladder is in closer relationship with the internal inguinal fossae, and hernia of the bladder is more often associated with direct than with oblique inguinal hernia. In aged patients the hernia is likely to be large, owing to relaxation of the musculature of the abdominal wall and muscular atony of the bladder.

When a paraperitoneal hernia of the bladder is discovered during operation, the treatment should vary according to the size of the hernia and its relation to the sac. If the hernia is small, it can be separated from the peritoneal sac by gauze dissection and invaginated into the abdomen, a purse-string suture being inserted through the floor of the inguinal canal to prevent recurrence. If the peritoneal sac covers a considerable portion of the bladder it should not be stripped off; excision should be performed around the bladder attachment on the inside, going up as high as the abdominal ring on the outside where the sac is quite free. The bladder is then invaginated and kept in place by a purse-string suture. Should the floor of the inguinal canal prove to be too weak and recurrence is expected, a flap from the anterior sheath of the rectus muscles may be turned outward and sutured to the internal oblique muscle. After taking care of the vesical hernia, operation is performed for the inguinal or femoral hernia.

Cystitis.—Mills [18] found few reports in the literature of gas-containing cysts or vesicles in the wall of the urinary bladder of the human being. Cystitis emphysematosa is a pathologic entity, being a localized lesion confined to the inner layers of the wall of the bladder and not a part of a generalized gas-producing bacterial infection. The name indicates an inflammatory condition of the bladder associated with the presence of gas vesicles in the tissues.

Mills reported three cases of cystitis emphysematosa occurring in men, disposing of the previously assumed limitation of this disease to women. The last cystoscopic examination of one patient was performed about four months before death; had cystitis emphysematosa existed at that time it might have been recognized. The other two patients did not present urinary symptoms for which a cystoscopy would have been indicated. The presence of marked evidence of both acute and chronic cystitis and of recent and old hemorrhage indicated that cystitis had existed for a considerable time before death.

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18. Mills, R. G.: Cystitis Emphysematosa: I. Report of Cases in Men, J. Urol. **23**:289 (March) 1930.

Drainage.—Lowsley [19] stated that suprapubic cystostomy as a preliminary procedure in preparing for a more radical operation has a definite value in surgery. The mortality rate is unusually low in cases in which preliminary drainage is done, considering the age and poor general condition of the patients on whom operations have been performed. This is particularly true in cases in which the prostate gland is enlarged and retention of urine is complete or partial. He noted that in many cases of prostatic enlargement the patients had received considerable trauma from attempts to pass instruments. In a few cases obstruction was so severe as to require evacuation of the bladder by immediate suprapubic cystostomy in preference to further attempts at intra-urethral manipulation, even though gradual decompression of the overdistended bladder is desirable whenever feasible.

There were 34 deaths (8.9 per cent) in 381 cases in which the bladder was drained as a preliminary to prostatectomy for benign hypertrophy. Fifty per cent of the deaths occurred in men aged more than 70 years, 6 of whom were more than 80. The youngest man who died was 50, and the oldest was 89, the average being 69.5 years. Death occurred after from one day to thirty-nine days, the average time being twelve and five-tenths days.

Kaufman [20] reviewed 300 diversified cases in order to study the use of the catheter in postoperative retention of urine. The incidence of retention was 17 per cent in these cases. The incidence of retention was highest following operations on pelvic and abdominal organs, varying from 18 per cent in operations for hernia to 31 per cent for hysterectomy. In a total of 34 abdominal operations, including operation on the gallbladder, stomach, appendix and large and small intestines, catheterization was performed on 23.5 per cent of the patients. In most cases the interval between operation and catheterization was twelve hours.

When a catheter is employed as a routine for postoperative retention, a urinary antiseptic should always be given as soon afterward as possible, and should be continued for at least from three to four days after catheterization ceases. A single catheterization does not require irrigation or instillation, but repetition over more than two or three days requires instillation once a day of either silver nitrate, 1:2,000, or acriflavine, 1:2,000, ½ ounce (14.175 Gm.). If it is necessary to

19. Lowsley, O. S.: Preliminary Drainage in Cases of Vesical Obstruction, with Particular Reference to Stricture of the Urethra, J. Urol. **23**:307 (March) 1930.

20. Kaufman, L. R.: Use of the Catheter in Retention, Am. J. Surg. **7**:785 (Dec.) 1929.

catheterize the patient for more than three days and more frequently than every eight to twelve hours, it is advisable to employ the retention catheter.

The causes of retention may be classified in three groups: 1. Organic obstructions of the bladder or urethra. In the male the most common causes of this type of obstruction are: stricture, especially of the membranous urethra; diseases of the prostate gland, usually hypertrophy; active inflammatory lesions of the prostate gland, particularly abscess; carcinoma of the prostate gland; carcinoma or tumor of the neck of the bladder, and calculus. Stricture also occurs in the female urethra. 2. Retention caused by disease of the central nervous system may be pathologic or functional. Pathologic obstruction may be caused by: neurosyphilis, which has a peculiar selective affinity in its changes of the cord on vesical function, producing retention or paralytic incontinence; fractures of the skull, spinal column or pelvis, or early lesions of the cord of pernicious anemia, of which retention may be one of the early predominating symptoms. Among the causes which may produce functional retention are coma induced by alcohol or drugs and certain infectious diseases which disturb the function of the nerve. 3. Retention in general surgical cases and in obstetric cases without previous lesions of the lower part of the urinary tract is difficult to explain. It occurs following operation on organs contiguous to or remote from the bladder or urethra and in all types of surgical cases; it occurs with sufficient frequency in obstetric practice to make it a prominent factor.

Foreign Bodies.—White [21] stated that foreign bodies in the bladder are sufficiently common to constitute disease. Foreign bodies may be introduced through the urethra or migrate from hollow abdominal viscera. Surgical accessories left behind after abdominal operations sometimes find their way into the bladder, and certain objects placed in the vagina may ulcerate their way through. Foreign bodies may occur in the bladder in relation to injury. The length of time during which a foreign body can remain in the bladder without causing marked symptoms and without becoming encrusted with salts is extremely variable. In some cases the distress is immediate and intense, and relief is sought before there is time for calculous deposit. In certain cases the foreign body has remained for many years in the bladder without symptoms and on removal has been found to be free from encrustations, whereas at other times the object becomes quickly coated with urinary salts. Largely as a result of infection, phosphates predominate among

21. White, H. P. W.: Foreign Bodies in the Urinary Bladder, Brit. J. Urol. **2**:27 (March) 1930.

the salts found on foreign bodies. There is often a definite act of deglutition on the part of the controlling musculature, with the result that there is a tendency for the foreign body in the urethra to go toward the bladder rather than to be extruded. Sometimes a foreign body in the bladder will perforate this viscus and cause a fistula with another organ. In one case reported a crochet needle caused a vesico-intestinal fistula.

There is also evidence that foreign bodies found in the urinary bladder may enter from the intestinal tract. Freeman removed, by cystotomy, an encrusted darning needle from the bladder of a child 4 years of age. The mother had seen the patient swallow the needle four months previously. Harrison removed from a man's bladder a stone, the nucleus of which was a whalebone mouthpiece of a pipe, which he had swallowed years before. Roberts removed a slate pencil from a man's bladder, the patient having swallowed it six months before. Concretions from the appendix which have become adherent to the bladder and have found their way into it have been identified as the nuclei of vesical calculi. Gallstones have behaved in a similar manner; in one case reported these stones were removed from the urinary bladder.

A group of foreign bodies that enter the bladder from adjacent parts is provided by the unabsorbable suture material used in operations on the uterus and other pelvic organs. Sometimes, after the lapse of several years, vesical symptoms arise, due to stones which are found to have unabsorbable thread sutures as nuclei.

Calculus forms in a large proportion of cases of wounds of the bladder resulting from projectiles. In thirty-two such cases calculus formed in ten, in all of which there was injury to the bony pelvis. Such fractures are doubly complicated by communication with the exterior and with the bladder. The urine reaches the site of fracture, and fragments of bone, often microscopic in size, enter the bladder. The persistence of a tract connecting the injured bone with the bladder, long after the external wound is healed, can often be demonstrated with a cystoscope or during operation. Confining the patient in the dorsal position will render the smallest bone particles a danger as nuclei for calculi. Pieces of shrapnel, rifle bullets or other foreign bodies may enter the bladder and be unsuspected until some outstanding symptom arises. A single projectile known to have entered the lower part of the body is not likely to be overlooked, but unsuspected fragments of shrapnel may exist without knowledge of their presence. Injuries received about the lower part of the body years before may be the unsuspected cause of vesical symptoms due to stone. A knife blade formed the nucleus of a large vesical calculus removed from a man

who twelve years previously had had an accident in which the knife blade entered in the region of the hip, broke off and could not be found afterward.

Litholapaxy is not a satisfactory procedure in cases in which the foreign body consists of metal, glass or bone and forms the nucleus of a stone, or when composed of softer substances such as wood, india rubber, chewing gum and paraffin, owing to the difficulty in disintegrating and evacuating the nucleus. Some of the foreign bodies float to the top of the fluid in the bladder when free from the anchoring effect of the stone. When, at cystoscopy, a stone is seen to be suspended from the wall of the bladder, it is safer to open the bladder to avoid the risk of grasping the wall in the lithotrite in attempting to grip the stone. Through the open wound the vesical mucosa may be examined for further sutures which may be on their way through the wall of the bladder.

[*Editorial Note.*—The fact that foreign bodies passed into the urethra are swallowed or are left behind at abdominal operations and find their way to the bladder, even as often as White's report would indicate, is of more than passing interest. The association of trauma and injury to the bladder and the encrustation of suture material is familiar to all. White's caution as to the use of the lithotrite in crushing the incrustations of foreign bodies is timely. Often much trauma may be necessary in disengaging the jaws of the lithotrite, and the cystostomy which the surgeon has tried to avoid will have to be performed under less favorable conditions than if it had been the initial procedure.]

PROSTATE GLAND

Hypertrophy.—Weiser [22] stated that the most common changes encountered in cases of adenoma of the prostate gland are infection, malignant degeneration and poor results following prostatectomy. Tuberculosis of the male genital tract, which is usually of hematogenous origin, is not uncommon, and it is not impossible to find tubercles in a hypertrophied gland. Tuberculosis of the epididymis and seminal vesicles is of significance in this relation. Examination of clinical material in Weiser's hospital disclosed eighty-seven cases of genital tuberculosis, in only one of which the prostate gland alone was involved. Genital tuberculosis is a disease of youth, and adenoma of old age.

A case was cited of a patient, aged 72, who had urinary retention. Examination showed normal external genitalia and a large prostate gland of boggy consistence. The urine contained traces of albumin, leukocytes, epithelial cells and various types of cocci. Prostatectomy

22. Weiser, A.: Tuberkulöse Infektion der hypertrophierten Prostata, Ztschr. f. urol. Chir. **28**:105, 1929.

was performed. The postoperative convalescence was slow. There was much coughing and expectoration, but bacilli of tuberculosis were never found. The suprapubic fistula was open at the end of five months. The slow recovery of the patient was explained by finding an old cavernous tuberculous process, with contiguous new miliary processes, in one lobe of an adenomatous, hypertrophied prostate gland.

Carcinoma.—Smith and Peirson [23] stated that the value of treatment for carcinoma of the prostate gland by high voltage roentgen rays has not yet been firmly established. From a study of twenty-five cases of carcinoma of the prostate gland treated by high voltage roentgen rays, they concluded that pain due to obstruction and to cystitis is not affected by irradiation and must be treated by appropriate measures. The roentgen rays will relieve other types of pain due to prostatic carcinoma and metastasis in most instances. The duration of relief is variable but usually lasts from one to six months after each series of treatments. In some cases the malignancy of the growth appears to be reduced, as evidenced by improvement in the patient's general condition and in the slowing up of the progress of the growth. Not more than three or four series of treatments, at intervals of from two to three months, should be given.

Tuberculosis.—Lowsley and Duff [24] stated that tuberculosis of the prostate gland is a frequent accompaniment of genital tuberculosis, but that it does not occur so often in urinary tuberculosis. Of the genito-urinary organs, the epididymis is most often affected by this disease; the kidney is next in frequency and is followed closely by the ureters and bladder. The seminal vesicles are occasionally the site of tuberculosis, usually after tuberculous epididymitis of long standing, and the prostate gland is least often affected. Primary tuberculosis of the gland is extremely rare. Tuberculosis of the genito-urinary tract is found at necropsy in a little more than 2 per cent of cases of pulmonary tuberculosis. In 70 per cent of the cases of urogenital tuberculosis there is coincident tuberculosis of the prostate gland, and in a small fraction of 1 per cent, primary tuberculosis of the gland.

The diagnosis of tuberculosis of the prostate gland is difficult, especially if it occurs in conjunction with benign adenomatous hypertrophy or if hard nodules are discovered on digital examination when the patient is of cancer age. If it is remembered that in all cases of urogenital tuberculosis the prostate gland is involved in 70 per cent, earlier diagnoses can be made and the chance for cure or of proportionate lengthening of life is increased.

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23. Smith, G. G., and Peirson, E. L.: The Value of High Voltage X-Ray Therapy in Carcinoma of the Prostate, J. Urol. **23**:331 (March) 1930.

24. Lowsley, O. S., and Duff, John: Tuberculosis of the Prostate Gland, Ann. Surg. **91**:106 (Jan.) 1930.

Surgical procedures are not ordinarily indicated in cases of tuberculosis of the prostate gland. In most cases in which the tuberculous gland has been removed, it was removed because of a mistake in diagnosis. It is Lowsley's practice to subject all patients to a continual period of observation and care. Some are given treatment by alpine light or by quartz light and others are given Koch's old tuberculin in graduated doses. Lowsley and Duff have used tuberculin for more than three years, not alone but as an adjunct or subsidiary agent in a regimen of treatment consisting of hygienic and dietetic measures, rest, mercury vapor, quartz light, heliotherapy and the urologic measures indicated. The general plan is to combine the urologic treatment with the tuberculous treatment to the extent it is applicable and adaptable to the needs of the individual patient.

Twenty-one of Lowsley and Duff's patients with tuberculosis of the prostate gland were operated on; only two operations were on the prostate gland. One of the two patients died a few weeks after leaving the hospital. Another patient improved under palliative treatment. Eight of the patients were given tuberculin and apparently were benefited. None of the patients was harmed by the tuberculin.

(To be Continued)